COMPARATIVE STUDY OF ORAL PREGABALIN VS GABAPENTIN FOR POST OPERATIVE ANALGESIA IN LOWER LIMB SURGERIES PERFORMED UNDER SPINAL ANAESTHESIA

Dissertation submitted to

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

In partial fulfilment for the award of the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

BRANCH X

DEPARTMENT OF ANAESTHESIOLOGY,

THANJAVUR MEDICAL COLLEGE,

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MAY 2018

CERTIFICATE

This is to certify that the dissertation entitled " **COMPARATIVE STUDY OF ORAL PREGABALIN VS GABAPENTIN FOR POST OPERATIVE ANALGESIA IN LOWER LIMB SURGERIES PERFORMED UNDER SPINAL ANAESTHESIA"** submitted by **Dr.S.SANDEEP** in partial fulfilment for the award of the degree of **Doctor of Medicine in Anaesthesiology** by the Tamilnadu Dr.M.G.R Medical University,Chennai is a bonafide record of the work done by him in the Department of Anaesthesiology, Government Thanjavur Medical College, during the academic year 2015 – 2018.

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submitted by Dr. S. SANDEEP **of**

Dept. of ANAESTHESIA **Thanjavur Medical College, Thanjavur**

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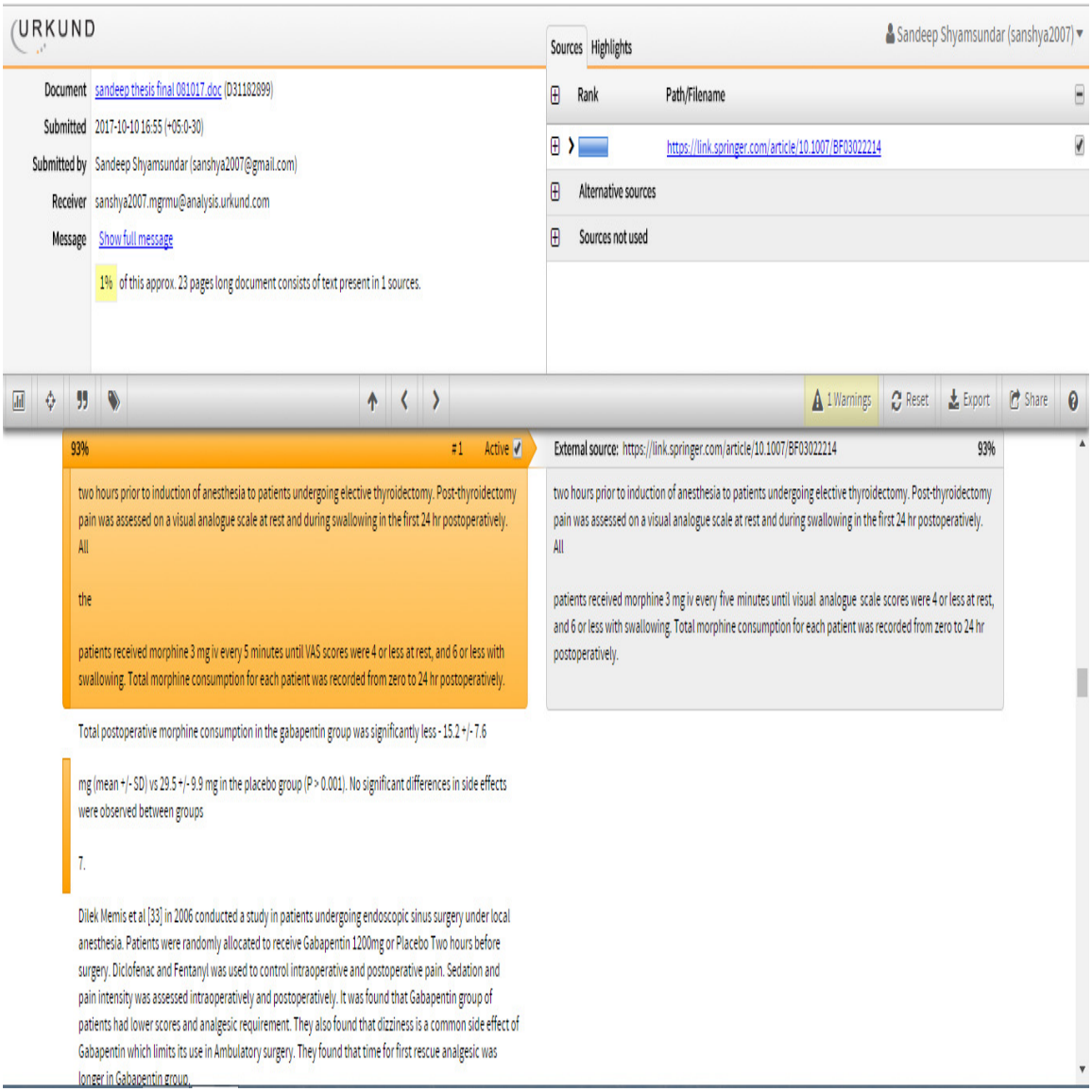
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Total postoperative morphine consumption in the gabapentin group was significantly less - 15.2 +/- 7.6
mg (mean +/- SD) vs 29.5 +/- 9.9 mg in the placebo group (P > 0.001). No significant differences in side effects were observed between groups
7.
Dilek Memis et al [33] in 2006 conducted a study in patients undergoing endoscopic sinus surgery under local anesthesia. Patients were randomly allocated to receive Gabapentin 1200mg or Placebo Two hours before surgery. Diclofenac and Fentanyl was used to control intraoperative and postoperative pain. Sedation and pain intensity was assessed intraoperatively and postoperatively. It was found that Gabapentin group of patients had lower scores and analgesic requirement. They also found that dizziness is a common side effect of Gabapentin which limits its use in Ambulatory surgery. They found that time for first rescue analgesic was longer in Gabapentin group.

CERTIFICATE - II

This is to certify that this dissertation work titled **"COMPARATIVE STUDY OF ORAL PREGABALIN VS GABAPENTIN FOR POST OPERATIVE ANALGESIA IN LOWER LIMB SURGERIES PERFORMED UNDER SPINAL ANAESTHESIA"** of the candidate **Dr.S.SANDEEP** with registration Number **201520201** for the award of **DOCTOR OF MEDICINE** in the branch of **ANAESTHESIOLOGY (BRANCH X).** I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **1** percentage of plagiarism in the dissertation.

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DECLARATION

I, **Dr.S.SANDEEP** solemnly declare that the dissertation titled "**COMPARATIVE STUDY OF ORAL PREGABALIN VS GABAPENTIN FOR POST OPERATIVE ANALGESIA IN LOWER LIMB SURGERIES PERFORMED UNDER SPINAL ANAESTHESIA"** is a bonafide work done by me at Thanjavur Medical College Hospital , Thanjavur , during 2015 – 2018.

The dissertation is submitted to **"The Tamilnadu Dr.M.G.R Medical University, Chennai"** Tamilnadu as a partial fulfilment for the requirement of M.D Degree examinations – Branch –X(Anaesthesiology) to be held in May 2018.

Place: Thanjavur

Date: **Dr. S.SANDEEP**

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I thank all the patients for willingly submitting themselves for this study.

INDEX

INTRODUCTION

Pain is defined as an unpleasant sensory and emotional experience which may be associated with actual or potential tissue damage[1]. Surgical trauma induces hyperalgesia which could lead to chronic pain in the post operative period when left unattended .

Post operative pain could be attributed to inflammation resulting from tissue trauma due to the surgical incision , tissue injury due to cauterization or direct nerve injury as a result of nerve transection, stretching or compression. Pro-inflammatory mediators released as a result of tissue injury such as prostaglandins, interleukins, cytokines and neurotrophins contribute to nociceptor sensitization. Also, a decrease in tissue pH and oxygen tension, and increased lactate concentration which may be persistent at the surgical site for several days play an important role in peripheral sensitization and spontaneous pain behavior following an incision [2].

Inadequately treated post operative pain may have various systemic implications on the patient such as tachycardia, hypertension, increased blood glucose, delayed wound healing and anxiety. Anxiety leads to a surge of catecholamines due to the stress response leading to tachycardia, hypertension and hemodynamic instability. Therefore the relationship between anxiety and pain is well established.

In fact, pain has been described as one of the causes for delayed discharge from the hospital after ambulatory surgery along with drowsiness and nausea/vomiting.[3]

Depression, psychological stress and late recovery are related to chronic post-surgical pain, which may occur even after a minor surgery. Hence, adequate post-operative pain relief must be an integral part of administration of anaesthesia. Major goal of postoperative pain management is to minimize the dose of medication, to lessen the side effects and provide adequate analgesia. This can be achieved by multimodal approach to pain management

Drugs such as IV paracetamol, IV diclofenac, COX 2 inhibitors and opioids do not necessarily meet all the requirements of post-surgical patients.[4] Opioids were used but their associated complications have led to the restriction in usage.

Multimodal analgesia therefore takes into account the exact mechanisms, new pharmaceutical products and other routes and modes of delivery of analgesics.

Based on the knowledge available regarding the management of post operative pain, this study was designed to compare the pre-emptive analgesic efficacy of oral gabapentin versus oral pregabalin in patients undergoing lower limb orthopaedic surgeries under spinal anaesthesia.

AIM OF THE STUDY

To evaluate and compare the preemptive analgesic efficacy of oral gabapentin vs oral pregabalin for postoperative analgesia in patients undergoing elective orthopaedic lower limb surgeries under spinal anaesthesia and to assess the incidence of adverse effects of gabapentin and pregabalin

PATHOPHYSIOLOGY OF NOCICEPTION

Definition of pain

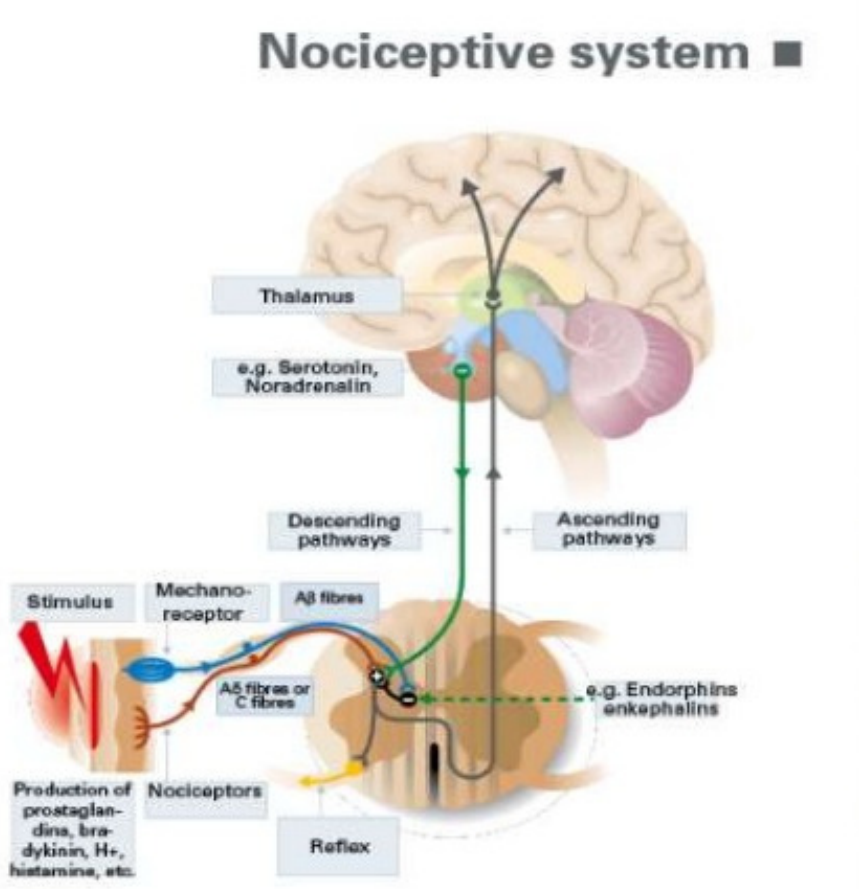
The international Association for the study of pain (IASP) defines pain as“an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”[5]

Physiology of pain[6]

The neural response to painful stimuli is defined as nociception.

The physiological processes involved in nociception are

- Transduction
- Transmission
- Perception
- Modulation



Picture demonstrating physiological process of nociception

TRANSDUCTION:

Tissue injury generates noxious stimuli which gets converted into electrical signals by a process known as transduction. This process occurs in nociceptors. Free nerve endings of unmyelinated C fibres and myelinated Aδ fibres act as nociceptors .

There are different types of nociceptors:

- mechanoreceptors : They respond to pinch and pinprick.
- Silent nociceptors : Respond only during inflammation
- Polymodal nociceptors: respond to pain temperature and pressure.

Nociceptors do not have the property to adapt to noxious stimuli which induces continued excitation leading to reduced threshold of nociceptors and is termed as sensitization of nociceptors.

Primary afferent neurons of nociception which are of pseudo unipolar variety have their cell bodies in dorsal root ganglia, with a peripheral terminal which ends as nociceptors and a central terminal which synapses with second order neurons in the dorsal horn of spinal cord.

The noxious stimuli can be chemical, mechanical or thermal. The stimulation leads to release of prostaglandin, bradykinin, serotonin, substance P, Potassium, and histamine from damaged tissues. These neurotransmitters released peripherally leads to sensitization of nociceptors to painful stimulus. Exchange of sodium and potassium ions at the cell membranes results in action potential and thereby generating pain impulse.

TRANSMISSION:

Transmission of pain impulse occurs from periphery to the spinal cord and then to thalamus and finally to the cerebral cortex.

Primary afferent fibres are the first order neurons which conduct pain impulse from nociceptors to dorsal horn neurons and are of two types: C fibres and Aδ fibres.

C fibres : They are unmyelinated with small diameter with a slow conduction velocity of 0.5–2m/s. They conduct more than one type of noxious stimuli and hence called as polymodal nociceptors. The C fibres conduct a diffuse, dull, slow onset pain known as second pain and they terminate on neurons of lamina I and II in dorsal horn of spinal cord.

Aδ fibres : They are myelinated with large diameter with a high conduction velocity of 2–20m/s. They respond to high intensity mechanical stimuli and hence called high threshold mechanoreceptors. They conduct a sharp, well localised, fast pain called as first pain. These fibres terminate on the neurons of lamina I and V in the dorsal horn of spinal cord. There is a synaptic cleft between the first order and second order neurons in the dorsal horn of spinal cord and the transmission of pain impulse across this cleft is mediated by release of excitatory neurotransmitters such as glutamate, substance P, calcitonin gene related peptide, adenosine triphosphate, bradykinin and nitrous oxide. Impulses from the first order neurons to the thalamus are conducted by the second order neurons. Second order neurons are of two types:

• **Nociceptive specific(NS)** and

• **Wide dynamic range neurons(WDR)**

NS neurons respond only to painful stimuli whereas WDR neurons respond to both noxious and non noxious input from Aβ, Aδ, and C fibres. Most of the second order neurons cross the midline to opposite side and ascend as spinothalamic tract(STT) to relay in thalamus. STT also sends fibres to reticular formation, nucleus raphe magnus and periaqueductal gray. STT can be divided into lateral and medial tracts. The lateral STT(neo spino thalamic) terminates in ventral posterolateral nucleus of thalamus transmitting pain and temperature and is responsible for emotional perception of pain.

Third order neurons are involved in transmitting the pain impulse from thalamus to somatosensory areas I & II in the postcentral gyrus and superior wall of the sylvian fissure in the cerebral cortex.

PERCEPTION:

The process by which pain produces conscious multidimensional experience is known as perception. Areas of cortex involved in pain perception include,

The reticular system – mediates motor response to pain.

Somatosensory cortex- Responsible for perceiving and interpreting the sensation and assessing the intensity, type and location of sensation and is

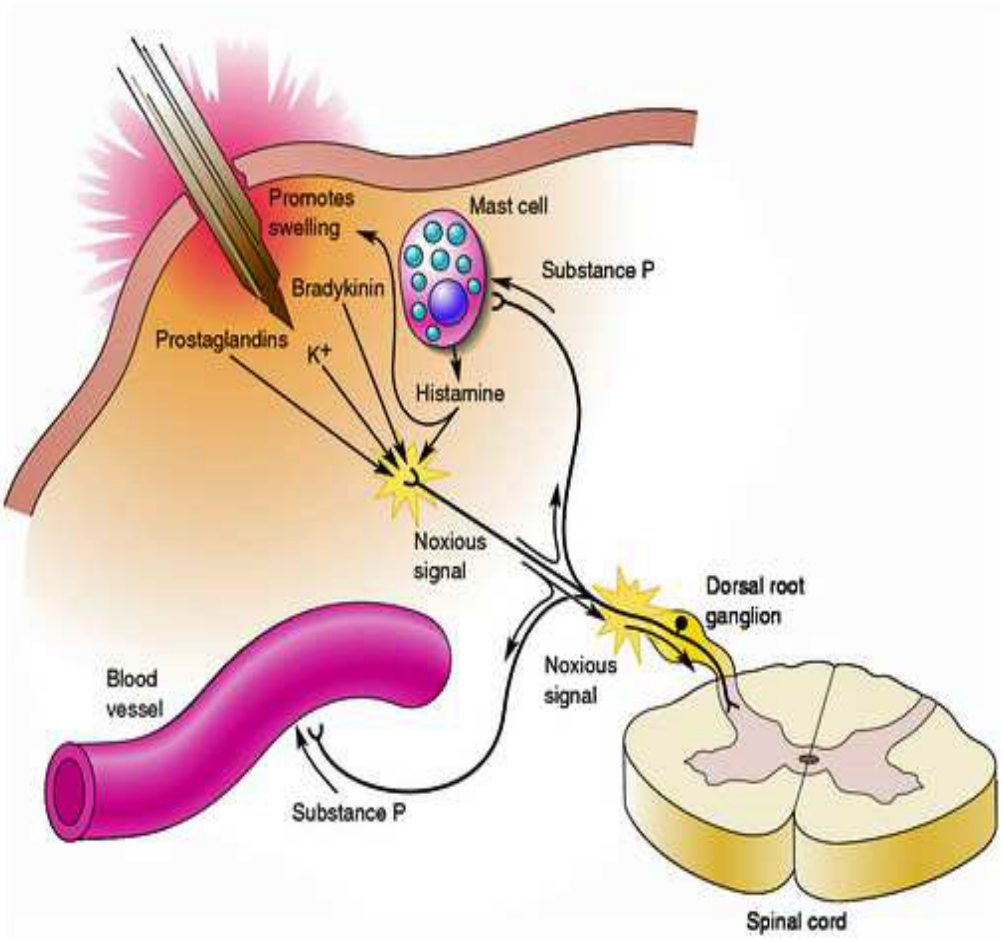
involved in comparing the sensation with past experiences and is responsible for memory of sensation.

Limbic system-Responsible for emotional and behavioural responses to pain.[7]

MODULATION:

Modulation is the process by which pain impulses produced are either inhibited or facilitated. It occurs peripherally in nociceptors and also in spinal cord and supraspinal structures. Stimulation of nociceptors by painful stimuli leads to continuous excitation resulting in sensitization. This leads to decreased threshold, decreased response latency, increase in frequency of response and continuous excitation even after cessation of stimuli .If it occurs in the site of injury it is known as primary hyperalgesia and in uninjured tissues it is called secondary hyperalgesia. This response is mediated by bradykinin, histamine and leukotrienes[7]

Pathophysiology of pain



Gate control theory of pain:

This was hypothesized by Ron Mezlack and Patrick in1962[8]. Pain perception is not due to direct activation of nociceptor alone and is modulated by different neurons. Dorsal horn of spinal cord acts as a gate by either inhibiting or allowing conduction of pain impulses. Pain signals carried by small nerve fibres are allowed to pass through while those carried by large nerve fibres are blocked.

Segmental inhibition:

Glycine and GABA are the inhibitory neurotransmitters which mediate segmental inhibition through GABA-B receptor activity thereby increasing potassium movement across the cell membrane.

Supraspinal inhibition:

Structures involved in supraspinal inhibition are periaqueductal gray, reticular formation and nucleus raphe magnus. Fibres from these sites act presynaptically on first order neurons and post synaptically on second order neurons. In this process monoamines like nor-adrenaline and serotonin act as neurotransmitters on spinal inhibitory interneurons to produce analgesia.

MULTIMODAL ANALGESIA

Kehlet and Dahl described the concept of combining multiple analgesic technique in 1993, to improve outcome following surgery[9]. This was introduced to maximize analgesic benefits and reduce the incidence of opioid-related adverse effects. Multimodal analgesia is achieved by combining different analgesics that act by different mechanisms at different sites in the nervous system, so that adequate analgesia is attained with lower doses and reduced incidence of side effects.

For maximum benefit, pain management must be initiated in the preoperative period itself , continued intra operatively and in the postoperative period. Also it is found to be effective in patients who are at risk of side effects with large doses of opioids such as the elderly, patients with obstructive sleep apnea and chronic pain.

BENEFITS

1.Effective analgesia due to synergistic action.

2.Less side effects due to lower dosage of drug used.

3.Faster recovery

MODES OF INTERVENTION

Acts by reducing nociceptive input

1.Peripherally acting drugs

A) Local anaesthetics: Local infiltration, Nerve Blocks, Spinal/Epidural blockade

B) NSAIDS: Cycloxygenase inhibitors

C) Glucocorticoids

2.Drugs acting in spinal cord

A) Opiates

B) NSAIDS

C) NMDA receptor antagonist

D) Gabapentinoids: gabapentin, pregabalin

3.Drugs acting centrally:

A) Opiates

B) Acetaminophen

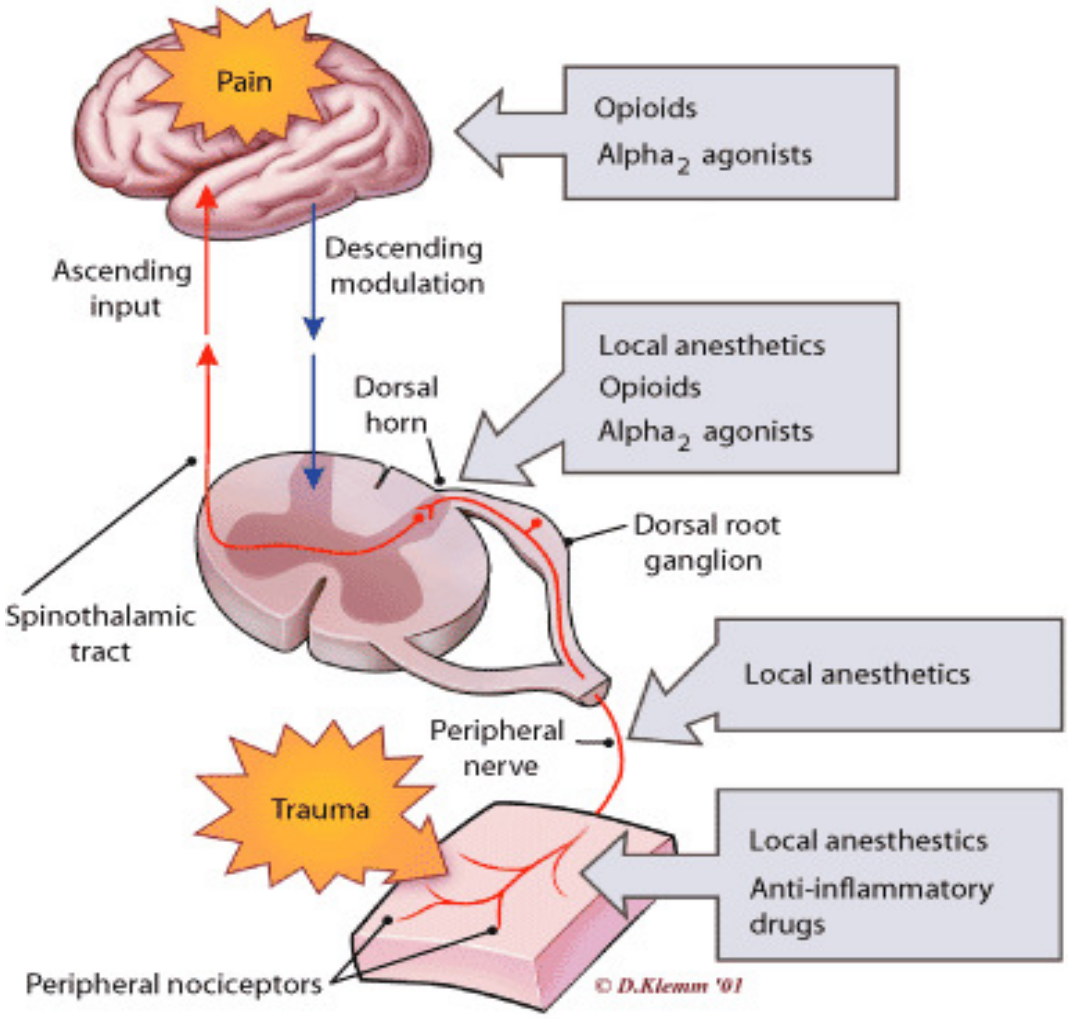
4.Drugs acting on descending pain pathway:

A) Tramadol

B) Alpha 2 agonists

C) 5 HT3 antagonists

MULTIMODAL ANALGESIA



PRE-EMPTIVE ANALGESIA

The concept of pain prevention was first introduced by Crile in 1913 and later developed by Wall and Woolf[10]. Pre-emptive analgesia is an anti nociceptive treatment that prevents establishment of altered processing of afferent input which amplifies postoperative pain.

GOALS

1.Prevents pain related pathologic modulation of central nervous system.

2.Decreases acute pain after tissue injury.

3.Inhibits persistence of post operative pain and development of chronic pain.

Effective preemptive analgesia uses multiple pharmacological agents to reduce nociceptor activation either by blocking or decreasing receptor activation and by inhibiting the production or activation of pain neurotransmitters.

Pain sensation from damaged tissues initiates a cascade of alterations in somatosensory system leading to increased responsiveness of both central and peripheral neurons. Due to these alterations, response to subsequent stimuli is increased thus amplifying pain. In preemptive analgesia, anti nociceptive treatment is started before the onset of pain stimulus and is operational during

the surgical procedure so that the physiological consequences of nociceptive transmission are reduced. Hence, preemptive analgesia is more effective than analgesic treatment initiated after surgery. It also reduces immediate post operative pain and prevents the development of chronic pain. Preemptive analgesia helps to prevent the neurological and biochemical consequences of noxious input to central nervous system.

PHARMACOLOGY OF GABAPENTIN

Gabapentin, a second generation anticonvulsant drug was introduced in 1993 for treatment of refractory partial seizures[11]. Later it was found to be effective in treating chronic pain conditions like post herpetic neuralgia, diabetic neuropathy, trigeminal neuralgia, HIV- related neuropathy, complex regional pain syndromes, inflammatory pain and malignant pain. Recently its use has been extended for management of postoperative pain.

Chemistry

Gabapentin,- 1-(amino methyl) cyclohexane acetic acid is a structural analogue of Gamma amino butyric acid (GABA), an inhibitory neurotransmitter. It is a white crystalline solid, highly charged at physiological pH and is freely soluble in water.

Molecular formula: C9 H17 NO2

Molecular weight: 171.24

P Ka1: 3.7

PKa2: 10.7

PHARMACOKINETICS

Oral bioavailability

Absorption of gabapentin is not dose dependant, because of a saturable L-aminoacid transport mechanism in the intestine. Hence oral bioavailability varies inversely with dosage. After a single dose of 300 and 600mg, bioavailability was found to be 60% and 40% respectively.

DISTRIBUTION

Extensively distributed in human tissues and fluid after administration. Volume of distribution is 0.6-0.8l/Kg. Concentration in adipose tissue is low because it is highly ionized at physiological pH. Less that 30% is bound to plasma proteins. Concentration in cerebrospinal fluid is 5-35% of those in plasma and in brain tissue it is 80% of those in plasma. After oral intake, peak plasma concentration is reached in 2-3 hours.

METABOLISM

Gabapentin is not metabolized in human body. Does not induce hepatic microsomal enzymes.

ELIMINATION

It gets eliminated unchanged in urine and the unabsorbed drug is excreted in faeces and renal clearance is related in a linear manner to creatinine clearance. Elimination half-life is 5-7 hours in patients with normal renal function and is unchanged by dose. It can be removed by hemodialysis.

DRUG INTERACTION

Cimetidine, a H2 receptor blocker decreases renal clearance when given concurrently.

Antacids reduce the bioavailability of gabapentin when given concurrently.

SPECIAL SITUATIONS

RENAL INSUFFICIENCY:

The half life of gabapentin is increased in patients with reduced creatinine clearance. Hence dose adjustment is necessary.

HEMODIALYSIS

In patients on dialysis, the half life of gabapentin is reduced.

AGE

With increasing age, renal clearance decreases. Hence reduction of dose is required in patients who have age related decline in renal function.

GENDER

Pharmacokinetic parameters for male and female are similar and hence there is no significant gender differences.

PREGNANCY & LACTATION

Gabapentin has been assigned to pregnancy category C. Animal studies have revealed fetal toxicity involving delayed ossification of several bones. There is no controlled data in human pregnancy. Gabapentin should be given when benefit outweighs risk. Gabapentin is secreted into human milk, hence used only when benefits outweigh the risk.

ANTI-NOCICEPTIVE MECHANISM

The exact mechanism is not known but most likely the anti nociceptive target of gabapentin is voltage gated calcium channels which are upregulated in the dorsal root ganglia and spinal cord after surgical trauma.

Gabapentin selectively binds to α2δ subunit of voltage gated calcium channels and inhibits calcium influx through these channels thereby inhibiting the release of excitatory neurotransmitters (glutamate, aspartate, substance P, calcitonin gene related peptide) from the primary afferent nerve fibres in the pain pathway.

Gabapentin does not affect the nociceptive threshold but has anti-allodynic and anti-hyperalgesic properties. Gabapentin activates the

descending nor adrenergic system and produces spinal nor epinephrine release, which acts on spinal α2 adrenoreceptor to produce analgesia.

Perioperative benefits

All perioperative applications are "off label" uses

Gabapentin

- provides perioperative anxiolysis

-It produces post operative analgesia

-It attenuates haemodynamic response to laryngoscopy and intubation

-It prevents chronic post surgical pain, postoperative nausea, vomiting and delirium.

ADVERSE EFFECTS

Sedation and dizziness are most common.

Asthesia, headache, nausea, ataxia, weight gain and amblyopia are other side effects.

PHARMACOLOGY OF PREGABALIN

Pregabalin, or S-(+)-3-isobutylgaba, was designed as a lipophilic analogue of GABA substituted at the 3-position to facilitate diffusion across the blood–brain barrier.[12]

3-Isobutylgaba exists in isomeric forms, with S-(+)-3-isobutylgaba (or pregabalin) being the pharmacologically active enantiomer. Although pregabalin is structurally related to GABA, it is inactive at GABA receptors and does not appear to mimic GABA physiologically. Moreover, pregabalin does not have affinity for receptor sites or alter responses associated with the action of several common drugs for treating seizures or pain, which suggests that its mechanism of action is novel. Its pharmacological effects result from its action as a ligand at the alpha-2- delta binding site, which is associated with voltage-gated calcium channels in the central nervous system (CNS).Pregabalin exhibits potent anticonvulsant, analgesic, and anxiolytic activity in various animal models

ABSORPTION

Pregabalin is rapidly and extensively absorbed after oral dosing in the fasting state, with maximal plasma concentrations occurring ~1 h after single or multiple doses, and steady state being achieved within 24–48 h after repeated administration

Maximal plasma pregabalin concentrations (C max) and total exposures (AUC) are proportional to dose after either single or multiple dosing . The oral bioavailability is high at ≥90% and is independent of dose. The mean elimination t1/2 of pregabalin is 6.3 hours and is also independent of dose and repeated drug administration . These findings of consistent dose-proportional pharmacokinetics, justify confidence in the prediction of dose–response relationships in clinical practice. In addition, the concentration–time profiles of pregabalin are similar after two- or three-times daily administration, which reflects the clinical findings that pregabalin administered via either dosing regimen resulted in similar efficacy. Moreover, the administration of pregabalin with food has no clinically relevant effect on the amount of pregabalin absorbed ,thus providing a dosing regimen that is uncomplicated by meals.

DISTRIBUTION, METABOLISM AND ELIMINATION

Pregabalin is a substrate of the system L transporter, which is responsible for the transport of large amino acids across the brain and gut. Consistent with this, pregabalin has been shown to rapidly penetrate the blood–brain barrier in preclinical studies conducted in mice, rats, and monkeys. This is of obvious importance for a drug that influences CNS activity. Pregabalin undergoes negligible metabolism in humans.

LACK OF DRUG INTERACTIONS

. The pharmacokinetic profile of pregabalin indicates that it should have a very low potential for drug– drug interactions. Since pregabalin is neither metabolized nor bound to plasma protein, there is no rationale to expect drug–drug interactions to occur via these mechanisms in clinical practice. Furthermore, studies using human liver microsomes have demonstrated that pregabalin does not affect the cytochrome P450 system at therapeutic doses, neither should it affect the metabolism of drugs eliminated via this route. As predicted from these findings, no drug interactions have been reported in pregabalin clinical studies to date, and none are anticipated in the future also.

POSTOPERATIVE PAIN ASSESSMENT METHODS

It is very important and mandatory to assess the degree of pain experienced by the patient in the postoperative period. Pain assessment is considered as an important vital sign in postoperative patients which must be done periodically. Postoperative pain assessment involves preoperative education of the patient about pain following surgery.

This preoperative education helps the patient to gain knowledge which alleviates the fear about pain and helps to reduce anxiety about pain. It also helps them to develop a positive approach towards pain thereby improving satisfaction of the patient.

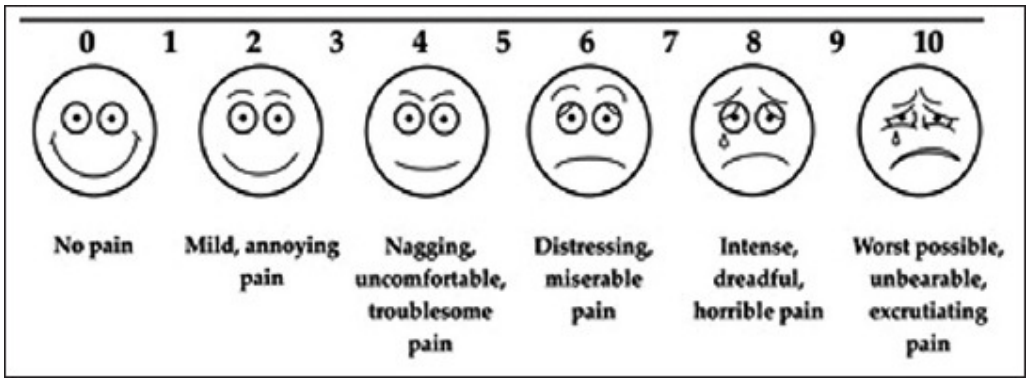
Postoperative pain assessment helps us to quantitate the intensity of pain, to formulate analgesic regimen and to assess the response to treatment given. There are a number of pain assessment methods but they must be simple and easily understandable by the patients.[13]

Commonly used pain scales are

- Visual analogue scale
- Numerical rating scale
- Verbal rating scale
- Wong baker faces rating scale

Visual analogue scale:

This scale is simple to use. It has a ten centimeter line with left end marked as no pain and right end marked as severe pain ever experienced. Patient is asked to mark a point on the line which corresponds to their pain intensity. Distance in centimeters recorded from left end of the line to upto patients mark is considered as the pain score. This scale is not useful in children, visually impaired persons and in those with cognitive impairment.

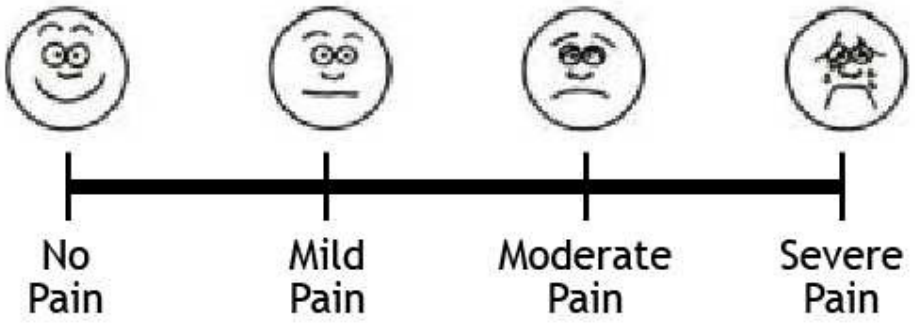


Numerical rating scale:

This scale closely resembles visual analogue scale. It consists of a ten centimeter line with left end marked as zero corresponding to no pain and, right end marked as ten corresponding to worst pain with numbers marked in between from one to nine. Thus it has eleven points on the scale. Patients are asked to point out a number on the scale which corresponds to their pain score.

Verbal rating scale:

Here the patients are asked to express their pain verbally as no pain, mild pain, moderate pain and severe pain. Small changes in pain intensity cannot be made out in this scale.



Wong baker faces rating scale:

This scale is useful in persons who cannot communicate properly and in children less than seven years of age.

REVIEW OF LITERATURE

1.**Hill et al** in 2001[15] conducted a trial comparing pregabalin to placebo and 400 mg of ibuprofen using a dental pain model. Study medication was administered postoperatively to patients who had undergone elective surgery to remove one or two third molars. The study was done to evaluate pregabalin at doses of 50 and 300 mg. Results proved that there were statistically significant differences in pain relief between the 300-mg pregabalin group and placebo. In addition, the 300-mg pregabalin group had a significantly longer duration of analgesia than the ibuprofen group and had the highest score on the patient global impression of study medication.

2.**Fassoulaki et al** in 2002[22] compared the analgesic effects of gabapentine and mexiletine given as post operative pain relief in 75 patients undergoing breast cancer surgery. They were randomized in a double-blinded manner, to receive mexiletine 600 mg/d, gabapentin 1200 mg/d, or placebo for 10 days. Anesthesia was standardized, and all patients had access to routine postoperative analgesics on demand. The visual analog scale score assessed pain at rest and after movement. Mexiletine and gabapentin reduced codeine consumption from the second to tenth day by 50% ($P = 0.029$; $P = 0.018$ and $P = 0.035$ for mexiletine versus control and gabapentin versus control comparisons, respectively). Total paracetamol consumption was also shown to be reduced during the same time ($P = 0.0085$; $P = 0.007$ and $P = 0.011$ for the

mexiletine and gabapentin groups when compared with the control, respectively). Pain at rest and after movement was reduced by both drugs on the third postoperative day. Pain after movement also was reduced by gabapentin between the second and fifth postoperative day.

3.**Jesper Dirks et al** in 2002[28] conducted a study in patients undergoing mastectomy to evaluate the effectiveness of Gabapentin on postoperative pain. Patients were divided into two groups to receive Gabapentin 1200mg or Placebo one hour before surgery. A standard technique of anesthesia was practiced. Postoperatively the pain intensity score and analgesic requirement was recorded for all patients and was found that pain scores with movement were significantly decreased at 2nd and 4th post-operative hours in patients who received Gabapentin. There was no difference in pain at rest and side effects between these groups.

4.**Turan et al** in 2004[14] conducted a study to assess whether preoperative administration of Gabapentin has a role in reducing the VAS scores and Tramadol requirement in patients undergoing hysterectomy through abdominal approach. Post-operatively, all patients were given Tramadol for control of pain in a standard manner. All of them were monitored for total dosage of analgesic required and for their pain intensity scores. It was concluded that the Tramadol consumption and VAS scores were lower in Group G patients.

5.**C.K.Pandey et al** in 2004[21] conducted a study to find out the effectiveness of preoperative Gabapentin in controlling post-operative pain and analgesic requirement. Study was performed in patients undergoing Lumbar discectomy. They were divided into Group G who received gabapentin 300mg and Group P were given Placebo capsules before 2 hours of surgery. Fentanyl was given at a dose of 2mg/Kg on demand intravenously for effective control of postoperative pain. Patients were monitored post-operatively for pain scores up to 24 hours. It was found that patients in Group G showed significantly lower pain scores and reduced requirement for Fentanyl in the postoperative period.

6.**Al Mujadi** et al in 2006[23] conducted a prospective, randomized, double-blind clinical trial, in which gabapentin 1200 mg or placebo was given two hours prior to induction of anesthesia to patients undergoing elective thyroidectomy. Post-thyroidectomy pain was assessed on a visual analogue scale at rest and during swallowing in the first 24 hr postoperatively. All the patients received morphine 3 mg iv every 5 minutes until VAS scores were 4 or less at rest, and 6 or less with swallowing. Total morphine consumption for each patient was recorded from zero to 24 hr postoperatively. Total postoperative morphine consumption in the gabapentin group was significantly less - 15.2 +/- 7.6 mg (mean +/- SD) vs 29.5 +/- 9.9 mg in the

placebo group ($P < 0.001$). No significant differences in side effects were observed between groups

7. **Dilek Memis et al** [33] in 2006 conducted a study in patients undergoing endoscopic sinus surgery under local anesthesia. Patients were randomly allocated to receive Gabapentin 1200mg or Placebo Two hours before surgery. Diclofenac and Fentanyl was used to control intraoperative and postoperative pain. Sedation and pain intensity was assessed intraoperatively and postoperatively. It was found that Gabapentin group of patients had lower scores and analgesic requirement. They also found that dizziness is a common side effect of Gabapentin which limits its use in Ambulatory surgery. They found that time for first rescue analgesic was longer in Gabapentin group.

8. **Tiippana et al** in 2007[19] selected 22 case studies on the preoperative administration of Gabapentin and their outcome was analyzed. It was found that one dose of Gabapentin ranging from 300-1200mg when given pre-operatively produced 20% to 60% of Opioid sparing effect. They also found that the dose of Gabapentin used did not have any effect on Opioid consumption in the post-operative period. The study revealed that the adverse effects of Opioids were significantly reduced by administration of Gabapentin per-operatively and sedation and dizziness were the most common side effects associated with use of Gabapentin.

9.**Agarwal et al** in 2008[20] conducted a prospective, randomized placebo controlled, double-blind study in sixty adults (16–60 yr) with ASA physical status I and II, of either sex undergoing elective laparoscopic cholecystectomy .Patients were divided into two groups of 30 each to receive either a matching placebo or pregabalin 150 mg, administered orally 1 h before surgery. Postoperative pain (static and dynamic) and postoperative patient-controlled fentanyl consumption were reduced in the pregabalin group compared with the placebo group (P,0.05). Side-effects were similar in both groups

10.**Saraswat et al**. in 2008[16] conducted a study to compare the efficacy of pregabalin and gabapentin with respect to increase in duration of analgesia, reduction in total post- operative requirements of analgesics and study side effects and complications. Sixty patients were randomly allocated to one of the two groups of thirty each. Patients in Group G were given single dose of gabapentin 1200mg, whereas in Group P were administered pregabalin 300mg one hour prior to administration of spinal anaesthesia. The total postoperative analgesic time was 8.98h in Group G whereas 14.17h in Group P (HS, $P < 0.001$). Total dose of analgesics in first 24h was 62.5mg in Group P and 72.5mg in Group G and was not significant ($P>.05$)..Dizziness and somnolence were the only side effects noticed in both groups

11.**Jokela et al** in 2008[24] evaluated the control of pain after perioperative administration of pregabalin 300 or 600 mg, compared with diazepam 10mg in 91 women scheduled for laparoscopic hysterectomy. Until the 1st postoperative morning, analgesia was provided by oxycodone using patient controlled analgesia. The visual analogue scale scores for pain and side effects and the amounts of the analgesics were recorded for three days after surgery. The doses of oxycodone during hours 0-12 after surgery were similar in the three groups, whereas the dose of oxycodone during hours 12-24 after surgery was smaller in the P600 group than in the P300 group (0.09 vs. 0.16 mg kg(-1); P=0.025). The total dose of oxycodone (0-24h after surgery) was smaller in the P600 group than in the D10 group (0.34 vs. 0.45 mg kg(-1); P=0.046).

12.**Panah Khahi et al** in 2011[25] conducted a study in patients undergoing orthopedic procedures involving tibia under spinal anesthesia. Patients were divided into two groups. Groups G received Gabapentin 300mg and Group P received Placebo capsules orally two hours before surgery. All patients were monitored postoperatively for VAS scores and analgesic requirement upto 24 Hours. It was found that VAS scores were less in Group G patients at Two hours post-operatively. There was no significant difference in VAS scores at all other time intervals between Group G and Group P. They also found that Gabapentin did not produce any side effect at this dosage.

13.**Anju Ghai et al** in 2011[17] conducted a study in 90 women undergoing abdominal hysterectomy who were anaesthetized in a standardized fashion. Patients received 300 mg pregabalin, 900 mg gabapentin or placebo, 1–2 hours prior to surgery. The primary outcome was analgesic consumption over 24 hours and patients were followed for pain scores, time to rescue analgesia and side effects as secondary outcomes. The diclofenac consumption was statistically significant between pregabalin and control groups, and gabapentin and control groups; however, pregabalin and gabapentin groups were comparable. Moreover, the consumption of tramadol was statistically significant among all the groups. Patients in pregabalin and gabapentin groups had lower pain scores in the initial hour of recovery. However, pain scores were subsequently similar in all the groups. Time to first request for analgesia was longer in pregabalin group followed by gabapentin and control groups.

14.**Rajendran et al** in 2014[26] conducted a randomized double blind study in 90 patients undergoing lower abdominal and lower limb surgeries. Patients were divided into three groups. Group G received tab gabapentin 900 mg, Group P received tab pregabalin 300 mg and Group C received placebo tablet orally 1 hour prior to surgery. All patients underwent surgery under spinal anesthesia using 0.5% Bupivacaine. Assessment of postoperative pain was made with visual Analogue Scale (VAS) score at 1, 2, 4, 6, 8,12, 18, and 24 hours post operatively. Injection tramadol 100 mg was given as rescue

analgesic intramuscularly when VAS score was > 7 in all the groups. Time to first rescue analgesics and number of rescue analgesics received were noted in all groups. The occurrences of side effects were noted in all groups. It was found that the tramadol as rescue analgesia consumption was less in pregabalin and gabapentin groups compared to control and was statistically significan ($P < 0.001$). Initial VAS scores were lower in pregabalin (3.2 ± 0.4) and gabapentin (3.63 ± 0.32) groups compared to control (6.60 ± 0.77) and was statistically significant ($P < 0.001$). Time to first rescue analgesia was significantly longer for pregabalin (24.6 hours) followed by gabapentin (20.76 hours) and control (4.93 hours) groups.

15.**Montaser et al in 2016**[18] conducted a study in which Sixty patients undergoing radical cystectomy were randomized into 4 groups: Group I: control (placebo) group, Group II: received pregabalin 300 mg 2 h preoperatively, Group III: received pregabalin 300 mg 2 h preoperatively and 12 h thereafter, Group IV: received pregabalin 600 mg 2 h preoperatively. Postoperative pain, time to first request of analgesia, and total morphine consumption were recorded. Results: VAS was significantly reduced in groups II, III, IV in comparison with group I immediately postoperative, and after 2 h ($P < 0.05$). Sedation score was significantly higher in groups II, III, IV compared to group I immediately postoperative ($P < 0.05$). First request of analgesia was significantly delayed in groups II, III, IV compared to control

group (P = 0.000). Total analgesic consumption was significantly reduced in groups II, III, IV compared to group I (P = 0.000). Group IV showed a significantly higher incidence of dizziness compared to group I. Conclusion: Peri-operative pregabalin at doses of 300 mg and 600 mg reduced postoperative opioid consumption and prolonged time to first request of analgesia and a single preoperative dose of 600 mg is superior in analgesia to others, without serious side effect

16. **Anil Verma et al**[34] conducted a study in patients undergoing abdominal hysterectomy under combined spinal epidural anesthesia. Patients were divided into two groups and were given Gabapentin 300mg or Placebo Two hours before surgery. Postoperatively analgesia was provided with 0.125% Bupivacaine epidurally on demand. The pain scores and number of epidural boluses received were recorded for all patients. It was found that the Gabapentin group had lower VAS scores and less number of epidural boluses to control post-operative pain.

MATERIALS AND METHODS

This study was a randomized, single blinded, prospective study conducted at the Department of Anaesthesiology, Thanjavur Medical College in association with the Department of Orthopaedics, Thanjavur Medical College.

Institutional Ethics Committee approval was obtained.

INCLUSION CRITERIA:

1. Patients undergoing elective lower limb surgeries under department of orthopaedics
2. American Society of Anaesthesiologists (ASA) physical status I and II patients
3. Age group 18 to 60 years
4. Male and female

EXCLUSION CRITERIA:

1. Patient refusal
2. History of allergy to gabapentin and pregabalin

3. History of drug and /or alcohol abuse

4. Patients who have been prescribed pregabalin or gabapentin for other indications

5. History of chronic pain and chronic daily intake of analgesics

6. History of epilepsy and other neurological disorders

7. Pregnancy and breast feeding mothers

8. Liver or renal disease

Patients satisfying inclusion criteria were randomly allocated by closed envelope method into three groups: Group P (Pregabalin group), Group G (gabapentin group) and Group C (placebo group). They were informed preoperatively about the visual analogue scale.

Patients in Group P received 300 mg of Pregabalin orally, Group G received Gabapentin 900mg orally and Group C patients received placebo capsules with sips of water two hours before surgery.

Inside the operating room, monitors (ECG, NIBP, Pulse oximeter) were connected. Bladder was catheterized to monitor urine output. Intravenous access established with 18G cannula.

All patients were preloaded with 10ml/kg of Ringer's lactate solution. Under strict aseptic precautions, 3ml of hyperbaric solution of 0.5%

bupivacaine with 25mcg of Inj Fentanyl was given in lumbar subarachnoid space using 25 Gauge Quincke needle.

At the end of surgery, patients were shifted to ward. VAS scores were assessed in the immediate postoperative period (0hr) and at 1, 2,3, 4, 6, 9,12 and 24 hours post operatively. Patients were given Inj.Tramadol 2mg/kg intramuscularly when the VAS score was 4 or greater. Dosage did not exceed 250 mg at one time and 600 mg per day. Time since spinal anaesthesia to first requirement of analgesic (T1), Total analgesic requirement in first 24 hours, VAS scores, Ramsay sedation score, side effects of the drug like dizziness, confusion, nausea, vomiting were recorded in first 24 hours postoperatively.

RESULTS

Ninety patients posted for orthopaedic lower limb surgeries of ASA I & II were taken up for the study. They were allocated randomly in a single - blind fashion into three groups in equal number of 30 each. Group C (placebo) received tablets of alike looking placebo, Group G (Gabapentin) received 900mg tablets of gabapentin,Group P (Pregabalin) received 300mg tablets of pregabalin 60 minutes prior to anaesthesia .A standard anaesthetic technique was followed in all patients. The patients were assessed by an observer in the postoperative period who was blinded for the group

At the end of study the data collected was analysed using statistical software package SPSS 20.0 . Data was analysed using one way analysis of variance(ANOVA),T test(within groups) and chi-square test. The results are expressed in terms of mean and standard deviation. P value of less than 0.05 is considered to be statistically significant.

Table 1: AGE DISTRIBUTION

Age in Years	Group P		Group G		Group C	
	Number	%	Number	%	Number	%
18-20	3	10	4	13	2	7
21-30	5	17	7	23	10	33
31-40	3	10	5	17	5	17
41-50	10	33	5	17	3	10
51-60	9	30	9	30	10	33
TOTAL	30	100	30	100	30	100
Range	30-55		30-50		30-50	
Mean	42.30		40.30		40.17	
SD	14.317		13.543		14.749	

Figure 1:Age Distribution

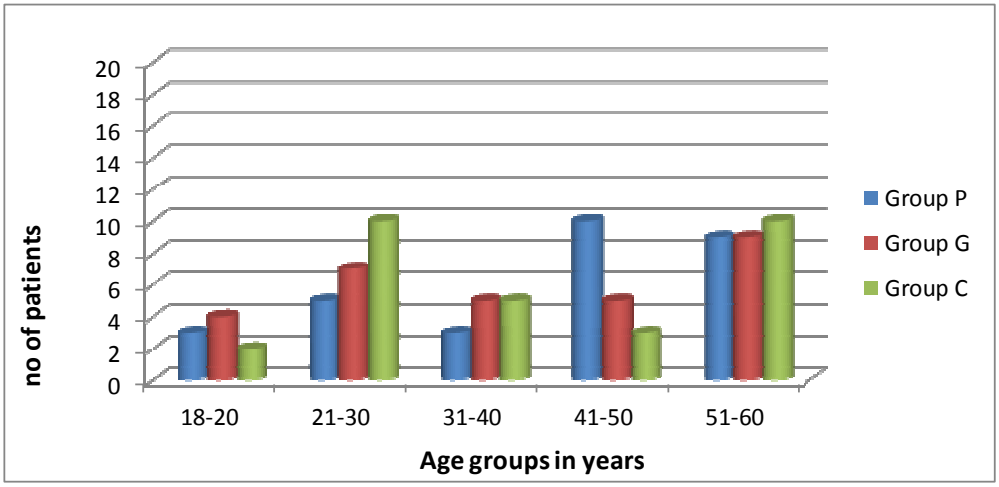


Table 1 shows the age distribution of the patients in all the three groups.The minimum age in Group P (Pregabalin group),Group G (Gabapentin group) and Group C (Placebo group) was 18 years.The mean age in Group P was 42.30±14.31 years, Group G was 38.30± 13.54 years and Group C was 40.17 ±14.74 years .There was no statistical significance between the age distribution in all 3 groups($p>0.05$).The three groups were comparable in age distribution

Table 2: Sex distribution

Group P (n=30)		Group G (n=30)		Group C (n=30)	
Male	**Female**	**Male**	**Female**	**Male**	**Female**
28	2	29	1	28	2

Figure 2: Sex distribution

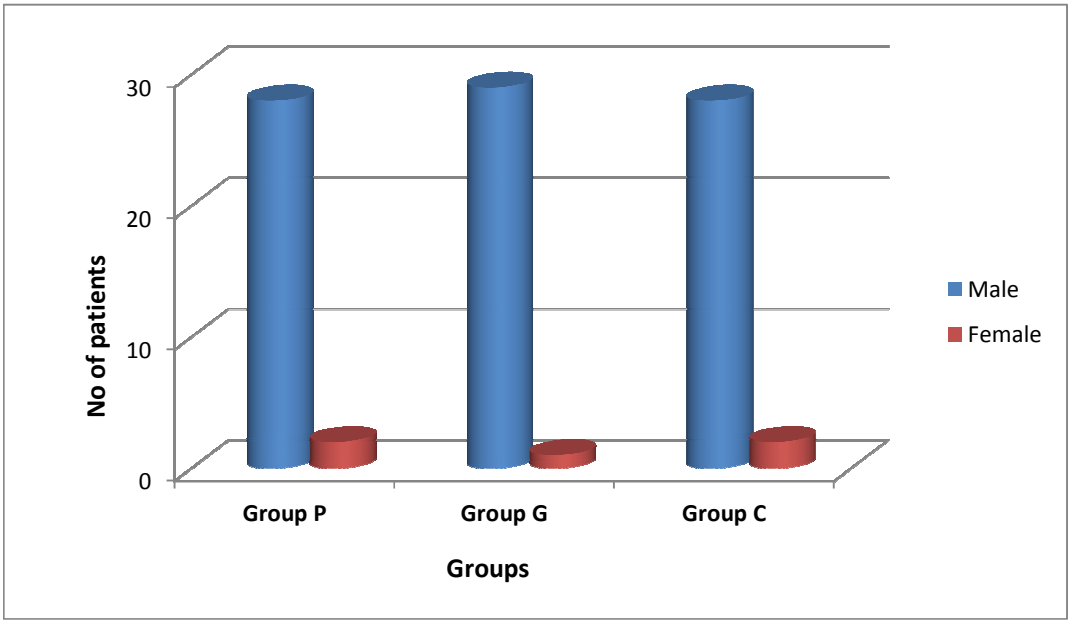


Table 2 and figure 2 show the gender distribution of all the patients in the three groups.There is no significant difference in the sex distribution between the three groups.(P>0.05)

Table 3: Height distribution

Height in cm	Group P		Group G		Group C	
	Number	%	Number	%	Number	%
141-150	2	7	0	0	1	3
151-160	12	40	16	53	8	27
161-170	16	53	14	47	19	63
171-180	0	0	0	0	2	7
TOTAL	30	100	30	100	30	100
Range	150-170		149-172		150-172	
Mean	161.70		160.77		163.30	
SD	4.647		4.158		4.907	

Figure 2: Height distribution

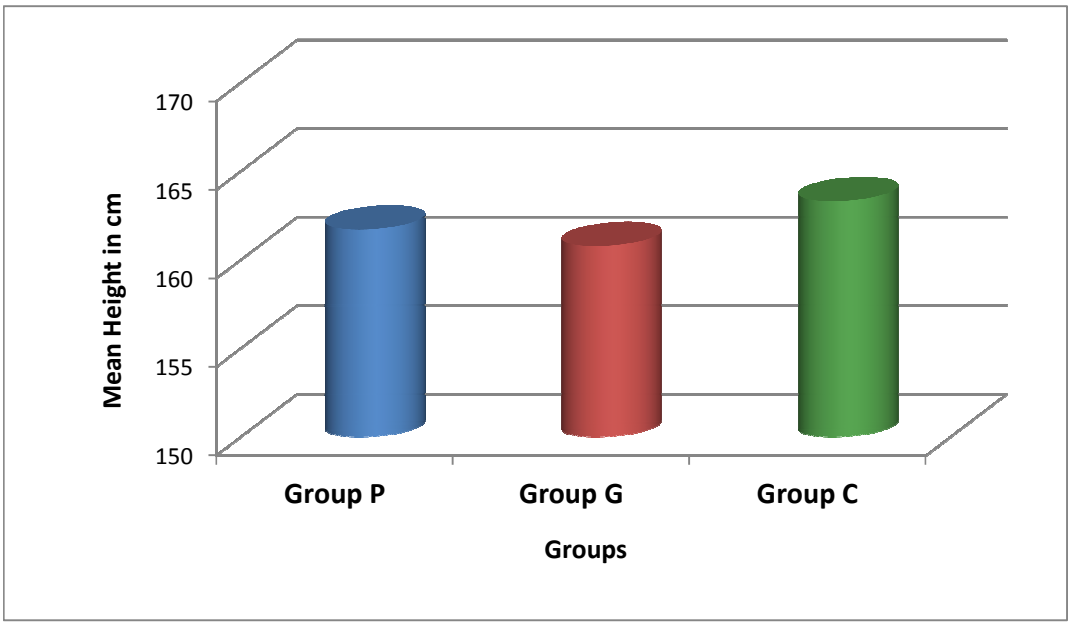


Table 3 and Figure 3 show the height distribution of patients.The mean height in Group P was 161.70± 4.647 cm,Group G was 160.77±4.158 cm and Group C was 163.30±4.907cm.There was no significant difference in the height of patients among the three groups .(P>0.05)

Table 4: Weight distribution

	Weight in kg		
	Group P	**Group G**	**Group C**
Mean	58.27	58.90	60.53
SD	6.596	6.804	6.394
Range	50-65	50-65	50-70

Figure 4: Weight distribution

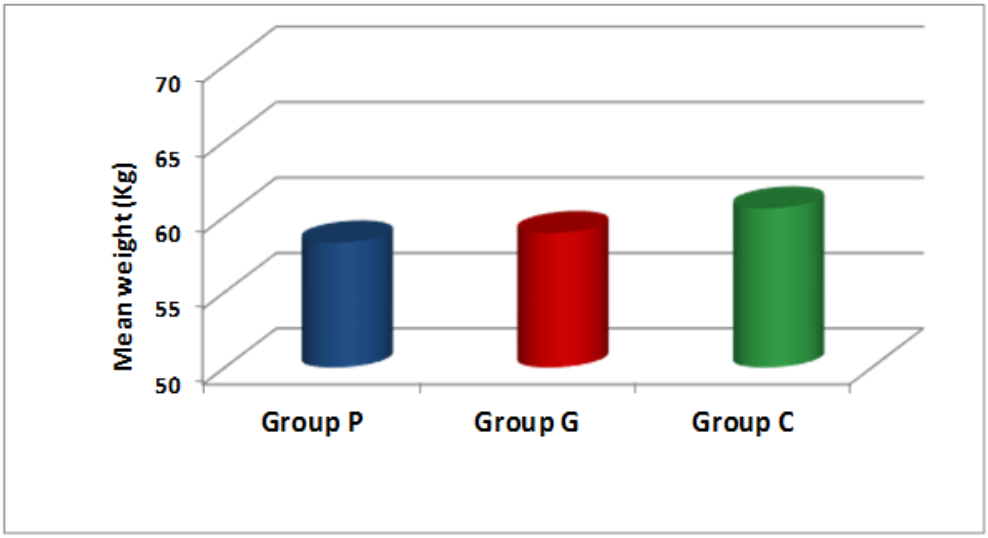


Table 4 shows the body weight distribution of patients.The mean body weight in Group P (Pregabalin group) was 58.27±6.596 kg, in Group G (Gabapentin group) was 58.90±6.804 kg and Group C(Placebo group) was 60.53±6.394 kg. The minimum body weight was 45 kg and the maximum weight was 72 kg.There was no significant difference in the body weight of patients among the three groups.(P>0.05)

Table 5: Duration of surgery

Duration in minutes	Group P	Group G	Group C
Mean	129	130.83	128.33
Range	90-180	90-180	90-170
SD	21.27	21.959	17.847

Figure 5: Duration of surgery

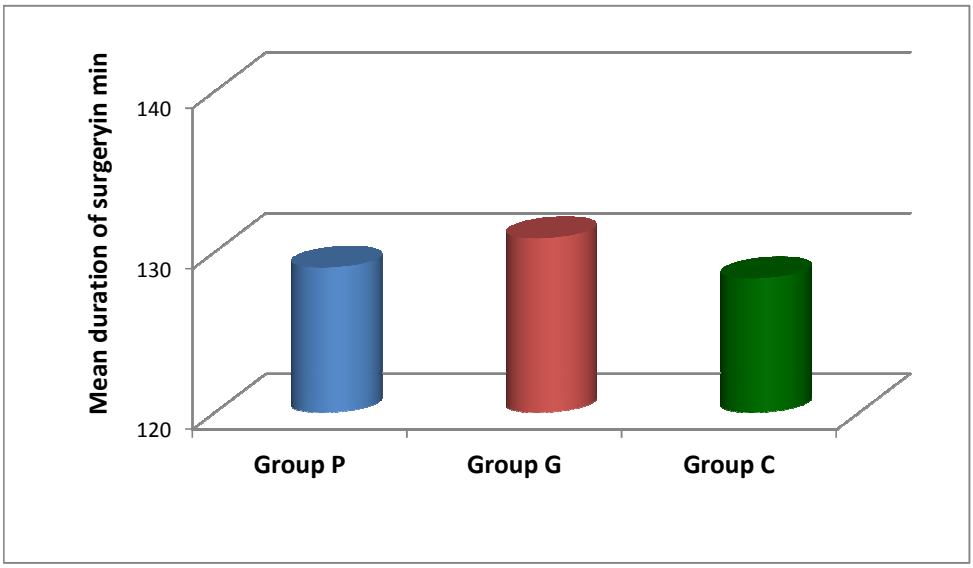
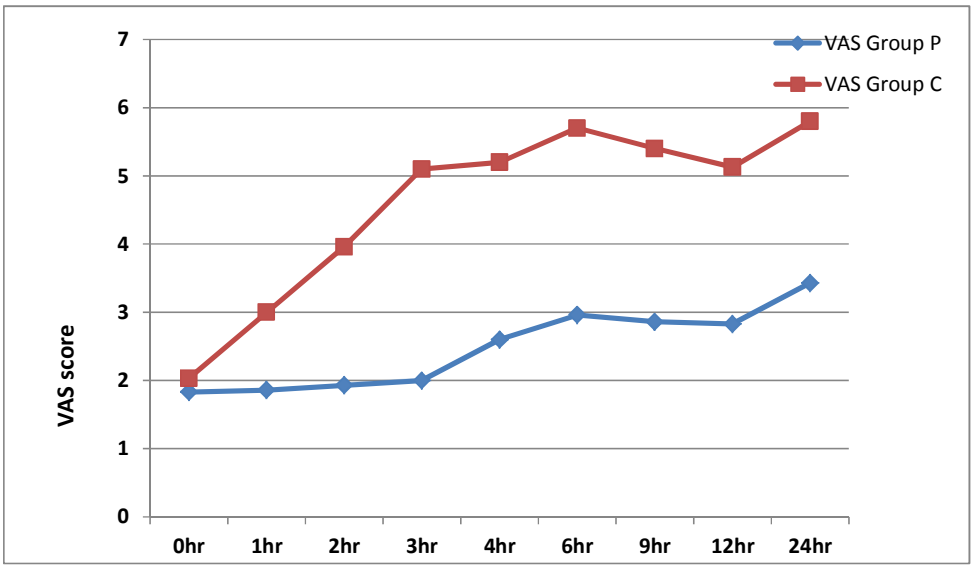


Table 5 and figure 5 show the mean duration of surgery in minutes in the three groups .The mean duration of surgery was 129 minutes with standard deviation(SD) of 21 for Group P,130.83 minutes with SD of 21 for Group G and 128.33 minutes with SD of 17 for Group C. There was no statistical significance among the three groups .(P>0.05)Thus the three groups were comparable with regard to duration of surgery

Table 6: Visual analogue scale (VAS) score of Group P vs Group C

VAS	Group P Mean (SD)	Group C Mean(SD)	P value
0 hour	1.83(0.507)	2.03(0.346)	P.08>0.05 Not Significant
1 hour	1.86(0.346)	3.0 (0.910)	P.000<0.05 Significant
2 hours	1.93(0.254)	3.96(0.928)	P.000<0.05 Significant
3 hours	2.0(0.263)	5.1(1.094)	P.000<0.05 Significant
4 hours	2.6(0.770)	5.2(0.379)	P.015<0.05 Significant
6 hours	2.96(1.098)	5.7(0.556)	P.000<0.05 Significant
9 hours	2.86(0.944)	5.4(1.192)	P.038<0.05 Significant
12 hours	2.83(0.913)	5.13(1.008)	P.039<0.05. Significant
24 hours	3.43(1.073)	5.8(0.664)	P.000<0.05 Significant

Figure 6: Visual analogue scale (VAS) score of Group P vs Group C



All patients were monitored for VAS scores at rest in the immediate postoperative period (0 hr), at 1, 2, 4, 6,9 12, and 24 hours postoperatively. In the immediate postoperative period (0 hr),the mean VAS score was found to be 1.83 in Group P and 2.03 in Group C with no statistically significant difference between the groups. This may be due to the effect of spinal anaesthesia.

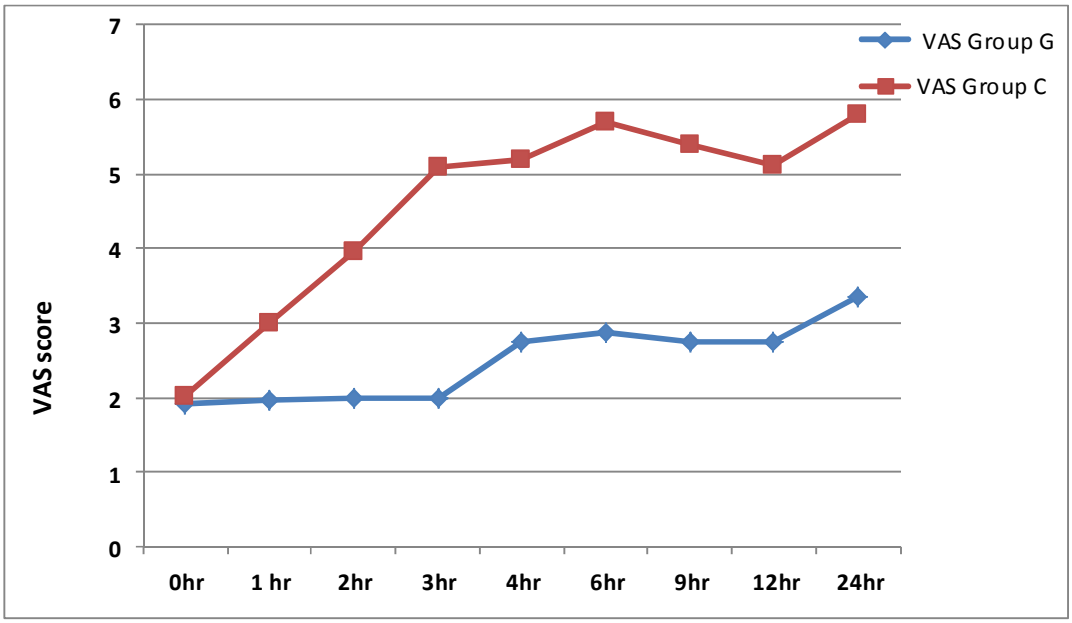
The mean VAS scores during postoperative period of 1, 2, 4, 6,9, 12 and 24 hours in group P patients were 1.86,1.93,2,2.6,3.36,3,2.83and 3.43 respectively

In Group C patients the mean VAS scores were 3,3.96, 5.1,5.2. 5.7, 5.4, 5.13 and 5.8 respectively. In all these time intervals ,the P value was less than 0.05 which is highly significant. This shows that there is a significant reduction in the mean VAS scores in patients receiving pregabalin premedication compared to control in the first 24 hours after surgery

Table 7: Visual analogue scale (VAS) score of Group G vs Group C

VAS	Group G Mean (SD)	Group C Mean(SD)	P value
0 hour	**1.93(0.254)**	**2.03(0.346)**	P.07>0.05 Not Significant
1 hour	**1.97(0.183)**	**3.0 (0.910)**	**P.000<0.05 Significant**
2 hours	**1.97(0.183)**	**3.96(0.928)**	**P.000<0.05 Significant**
3 hours	**2.0(0.00)**	**5.1(1.094)**	**P.000<0.05 Significant**
4 hours	**2.76(1.104)**	**5.2(0.379)**	**P.007<0.05 Significant**
6 hours	**2.87(0.937)**	**5.7(0.556)**	**P.015<0.05 Significant**
9 hours	**2.76(1.022)**	**5.4(1.192)**	**P.018<0.05 Significant**
12 hours	**2.76(0.898)**	**5.13(1.008)**	**P.025<0.05. Significant**
24 hours	**3.36(0.980)**	**5.8(0.664)**	**P.000<0.05 Significant**

Figure 7: Visual analogue scale (VAS) score of Group G vs Group C

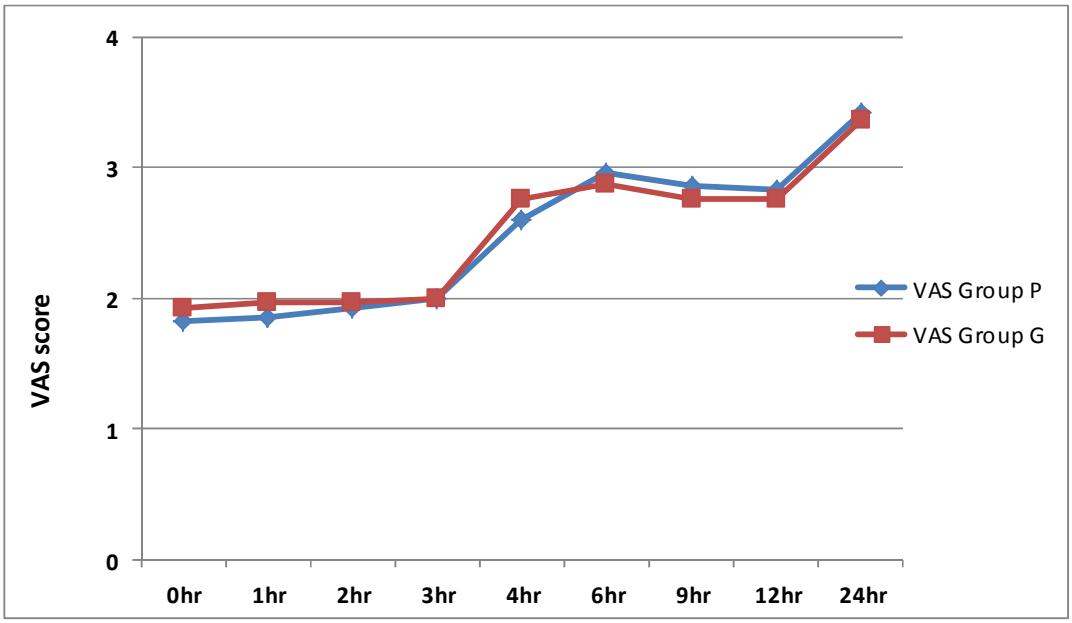


In the immediate postoperative period (0 hr),the mean VAS score was found to be 1.93 in Group G and 2.03 in Group C with no statistically significant difference between the groups. This may be due to the effect of spinal anaesthesia. The mean VAS scores during postoperative period of 1, 2, 4,6,9,12 and 24 hours in group G patients were 1.97,1.97,2,2.76,2.87,2.76,2.56 and 3.26 respectively. In Group C patients the mean VAS scores were 3,3.96, 5.1, 5.2. 5.7, 5.4, 5.13 and 5.8 respectively. In all these time intervals, the P value was less than 0.05 which is highly significant.This shows that there is a significant reduction in the mean VAS scores in patients receiving gabapentin premedication compared to control in the first 24 hours after surgery

Table 8: Visual analogue scale (VAS) score of Group P vs Group G

VAS	Group P Mean (SD)	Group G Mean (SD)	P value
0 hour	1.83(0.507)	1.93(0.254)	P.07>0.05 Not Significant
1 hour	1.86(0.346)	1.97(0.183)	P.167>0.05 Not Significant
2 hours	1.93(0.254)	1.97(0.183)	P.561>0.05 Not Significant
3 hours	2.0(0.263)	2.0(0.00)	P1.000>0.05 Not Significant
4 hours	2.6(0.770)	2.76(1.104)	P.500>0.05 Not Significant
6 hours	2.96(1.098)	2.87(0.937)	P.063>0.05 Not Significant
9 hours	2.86(0.944)	2.76(1.022)	P.362>0.05 Not Significant
12 hours	2.83(0.913)	2.76(0.898)	P.259>0.05 Not Significant
24 hours	3.43(1.073)	3.36(0.980)	P.532>0.05 Not Significant

Figure 8: Visual analogue scale (VAS) score of Group P vs Group G



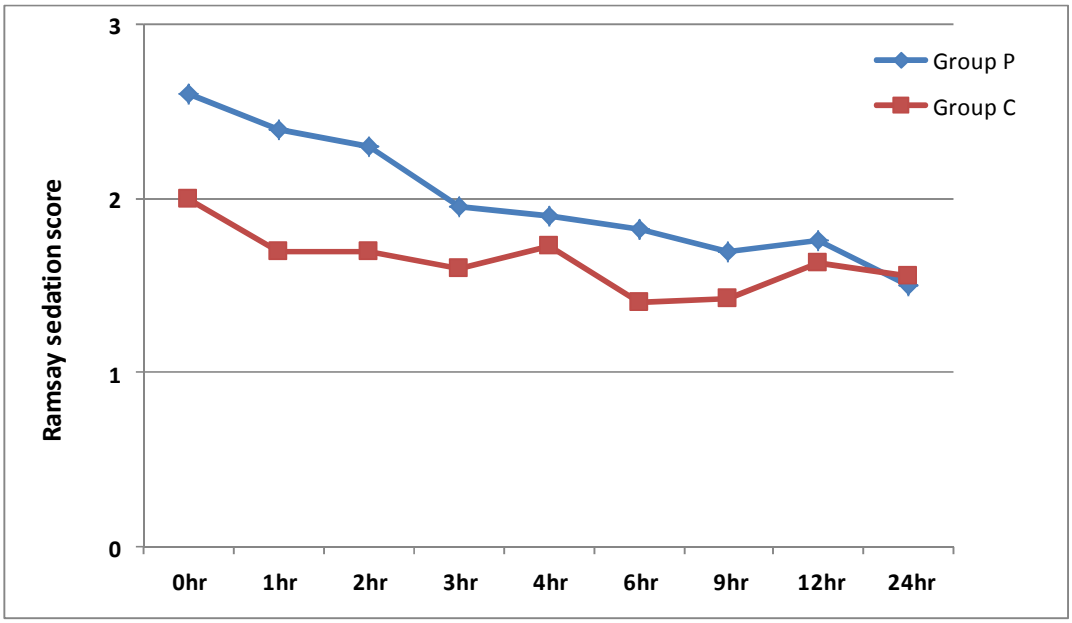
The mean VAS scores during postoperative period of 0,1, 2, 4, 6,9, 12 and 24 hours in group P patients were 1.83, 1.86,1.93,2,2.6,3.36,3,2.83and 3.43 respectively

In Group G patients the mean VAS scores were 1.93,1.97,1.97,2,2.76, 2.87, 2.76, 2.76 and 3.26 respectively. The P value at all these time intervals was > 0.05 which was not statistically significant. This shows that there is no significant difference between the analgesic properties of pregabalin and gabapentin.

Table 9: Ramsay sedation score. Group P vs Group C

Time	Group P Mean (SD)	Group C Mean(SD)	Pvalue
0 hour	2.60(0.312)	2.0(0)	P.004<0.05 Significant
1 hour	2.4(0.123)	1.7(.466)	P.001<0.05 Significant
2 hours	2.3(0.325)	1.7(.466)	P.001<0.05 Significant
3 hours	1.96(.183)	1.6(.498)	P.000<0.05 Significant
4 hours	1.9(.305)	1.73(.450)	P.018<0.05 Significant
6 hours	1.83(.490)	1.40(.498)	P.000<0.05 Significant
9 hours	1.7(.466)	1.43(.504)	P.078>0.05 Not Significant
12 hours	1.76(.430)	1.63(.490)	P.267>0.05 Not Significant
24 hours	1.50(.509)	1.56(.254)	P.345>0.05 Not Significant

Figure 9: Ramsay sedation score.Group P vs Group C



Postoperatively all patients were assessed for the level of sedation using Ramsay sedation score periodically at 0, 1, 2, 4, 6, 9,12, and 24 hours. The mean sedation scores at 0, 1, 2,3, 4, 6 hours of postoperative period in group P were 2.6, 2.4, 2.3, 1.96, 1.9, 1.83.In Group C, the scores were 2,1.7,1.7,1.6,1.73 and 1.4 respectively. The P value at all time intervals upto 6 hrs was less than 0.05 which was highly significant.

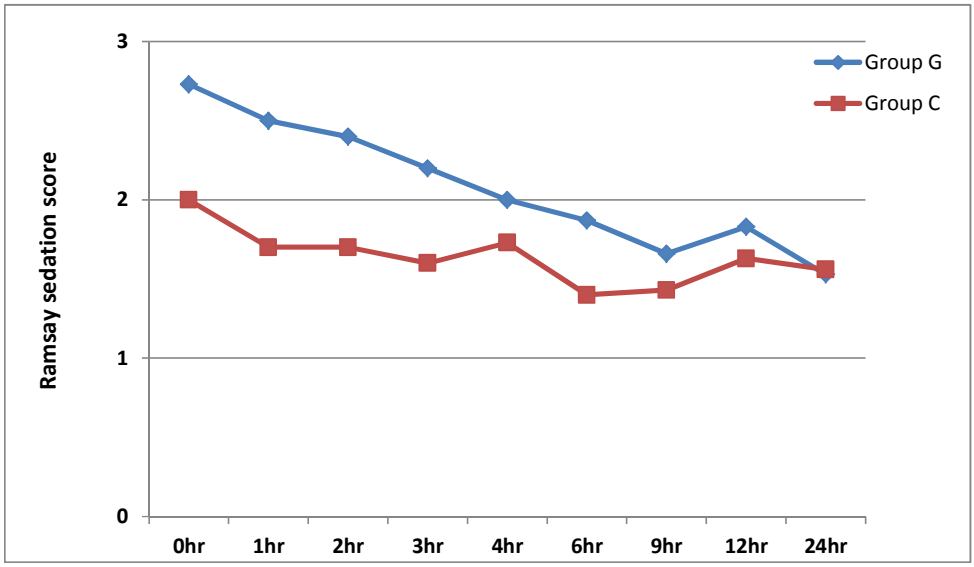
This shows that the level of sedation was significantly higher in group P patients compared to Group C upto 6 hours in the postoperative period.

However, the scores at 9,12 and 24 hrs were not statistically significant among the 2 groups. This shows that the sedation effect of pregabalin is not significant beyond 6 hrs postoperatively

Table 10: Ramsay sedation score. Group G vs Group C

Time	**Group G Mean(SD)**	**Group C Mean(SD)**	**P value**
0 hour	2.73(.407)	2.0(0)	P.000<0.05 Significant
1 hour	2.5(.498)	1.7(.466)	P.000<0.05 Significant
2 hours	2.4(.305)	1.7(.466)	P.000<0.05 Significant
3 hours	2.2(.183)	1.6(.498)	P.000<0.05 Significant
4 hours	2.00(0)	1.73(.450)	P.002<0.05 Significant
6 hours	1.87(0.183)	1.40(.498)	P.001<0.05 Significant
9 hours	1.66(.479)	1.43(.504)	P.071>0.05 Not Significant
12 hours	1.83(.592)	1.63(.490)	P.159>0.05 Not Significant
24 hours	1.53(.681)	1.56(.254)	P.16>0.05 Not Significant

Figure 10: Ramsay sedation score.Group G vs Group C



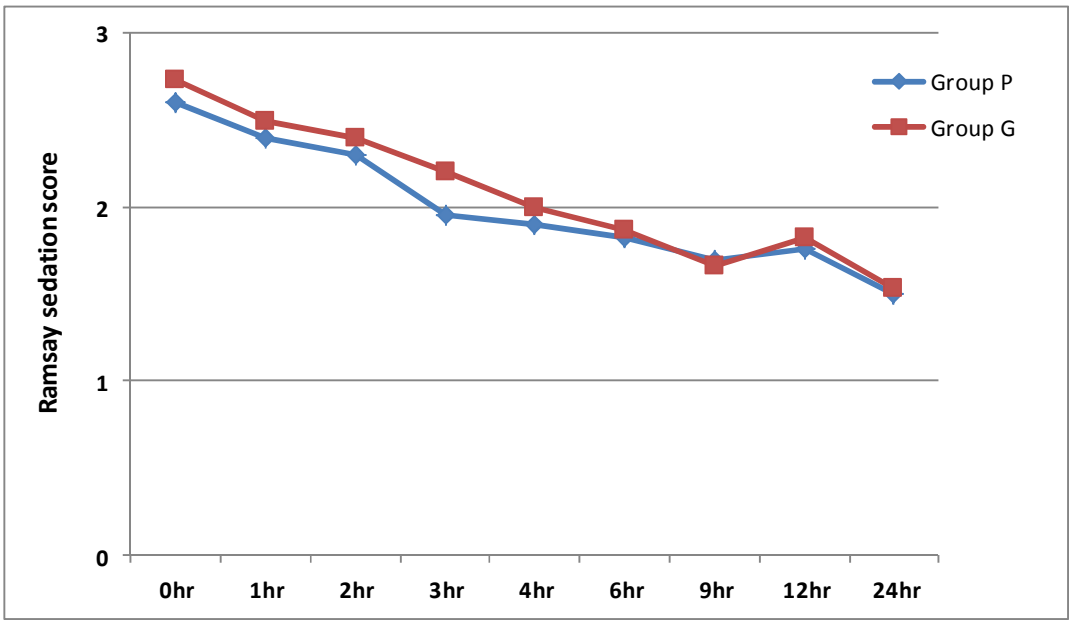
The mean sedation scores at 0, 1, 2,3, 4, 6 hours of postoperative period in group G were 2.73,2.5, 2.4, 2.2, 2, and 1.97 respectively. In Group C, the scores were 2,1.7,1.7,1.6,1.73 and 1.4 respectively .The P value at all time intervals upto 6 hrs was less than 0.05 which is highly significant

This shows that the level of sedation was significantly higher in group G patients compared to Group C upto 6 hours in the postoperative period. However, the scores at 9,12 and 24 hrs were not statistically significant among the 2 groups. This shows that the sedation effect of gabapentin is not significant beyond 6 hrs postoperatively

Table 11: Ramsay sedation score. Group P vs Group G

Time	**Group P Mean (SD)**	**Group G Mean(SD)**	**Pvalue**
0 hour	2.60(0.312)	2.73(.407)	P.261>0.05 Not Significant
1 hour	2.4(0.123)	2.5(.498)	P.352>0.05 Not Significant
2 hours	2.3(0.325)	2.4(.305)	P.078>0.05 Not Significant
3 hours	1.96(.183)	2.2(.183)	P.98>0.05 Not Significant
4 hours	1.9(.305)	2.00(0)	P.73>0.05 Not Significant
6 hours	1.83(.490)	1.87(0.183)	P.786>0.05 Not Significant
9 hours	1.7(.466)	1.66(.479)	P.620>0.05 Not Significant
12 hours	1.76(.430)	1.83(.592)	P.831>0.05 Not Significant
24 hours	1.50(.509)	1.53(.681)	P.405>0.05 Not Significant

Figure 11: Ramsay sedation score. Group P vs Group G

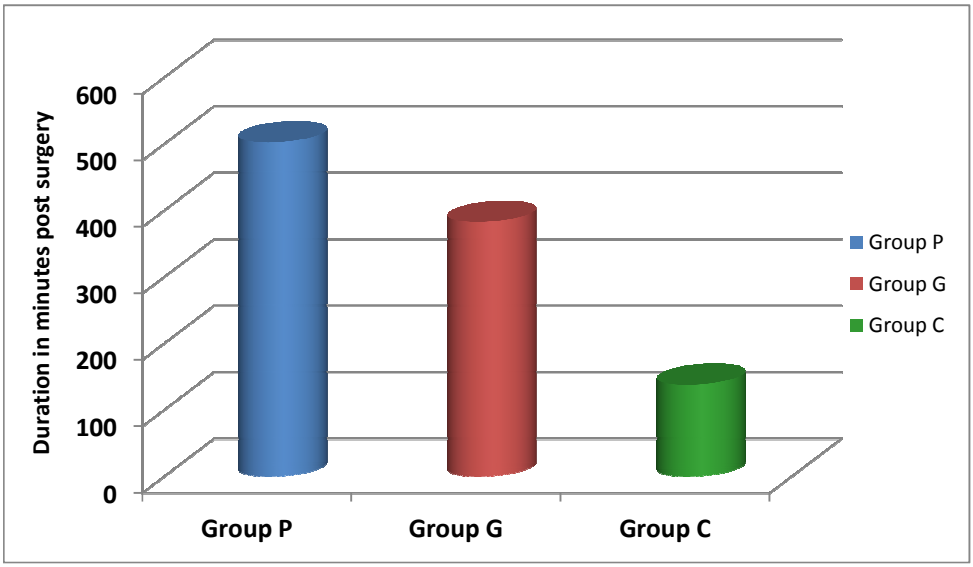


The mean sedation scores of Group P and Group C at all time intervals were comparable as the P value was greater than 0.05.Hence, Pregabalin and Gabapentin have similar sedating effects in the post operative period

Table 12: Time of rescue analgesic (T1)

Duration in minutes from the end of surgery	Group P	Group G	Group C	P value
Mean	502.3	382.6	137.8	**0.000**
SD	101.087	119.162	44.483	
Range	220-550	220-570	60-205	

Figure 12: Time of rescue analgesic (T1)



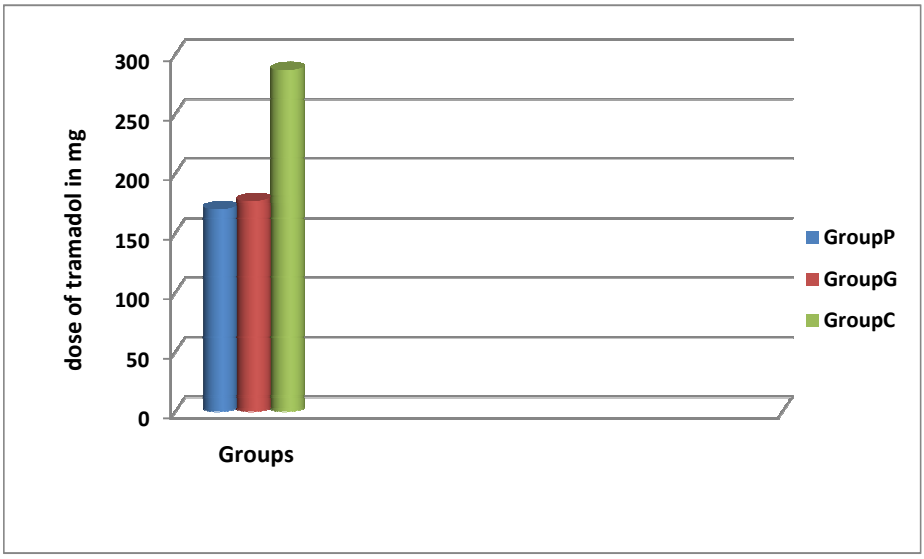
Postoperatively all patients were monitored for VAS scores periodically. When the VAS score at rest is 4 or greater, patients were given Tramadol 2mg/kg intravenously as initial dose. So T1 is the time interval between providing spinal anaesthesia and administration of first dose of tramadol. It was found that this Time interval was 137.8minutes in group C, 502.3 minutes in Group P and 382.6minutes in group G. The P value was found to be 0.00, which is considered significant. This indicates that T1 score was significantly greater in group C compared to group P and Group G. Hence Gabapentin and Pregabalin give prolonged post operative pain relief compared to control

The T 1 score of Pregabalin group was found to be greater than that of gabapentin with a P value.016 <0.05 which was highly significant. Hence Pregabalin provides more prolonged pain relief compared to gabapentin

Table 13: Total dose of Tramadol administered in 24 hours post surgery

Dose in mg	Group P	GroupG	Group C	
Mean(SD)	170(46.609)	176.7(50.401)	286.7(34.575)	**P.000<0.05 Significant**
Range	100-200	100-300	100-300	

Figure 13: Total dose of Tramadol administered in 24 hours post surgery



Postoperative analgesia was provided with intravenous tramadol for all patients. Initial dose of tramadol is 2mg/kg intravenously, when patient's VAS score is 4 or more. Subsequently tramadol was given at a dose of 2 mg/kg when the VAS score was 4 or more, or on patients demand. Care was taken not to exceed the limit of 250mg/dose and 600mg/day. Total dosage of Tramadol required for each patient during postoperative period upto 24 hours was calculated. In group C patients, average dose of tramadol required was 286.7 mg In group P, the dosage required was 170mg.In group G the dosage required was 176.7mg. The P value was found to be 0.000 which is highly significant.. Hence it was found that total tramadol consumption was significantly lower in group P and group G patients compared to group C.

Table 14 :Incidence of adverse effects

Adverse effects	Group P(n=30)	GroupG(n=30)	Group C(n=30)
Nausea	0	2	5(16%)
Vomiting	0	0	3(10%)
Giddiness	4(13%)	3 (10%)	0

Figure 14: Incidence of adverse effects

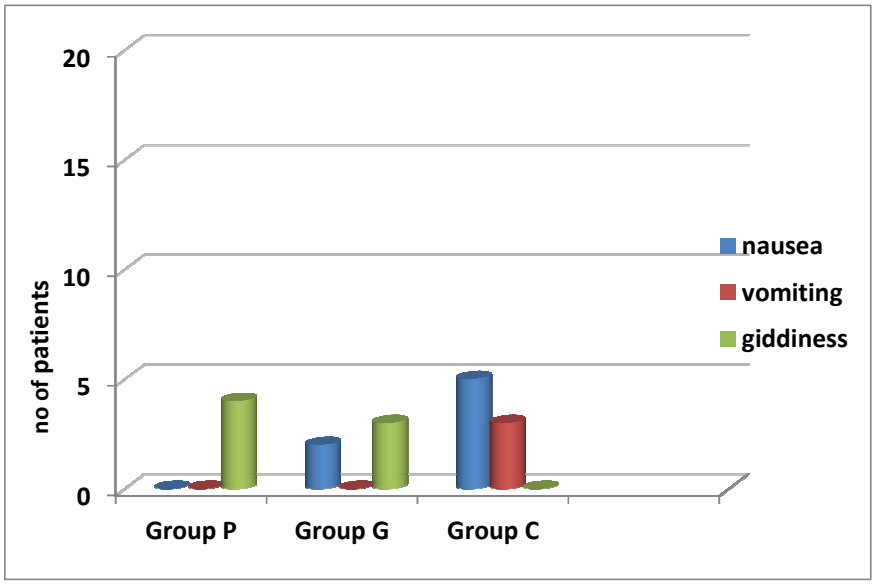


Table 14 and figure 14 show the incidence of side effects in the three groups. In group G, 3 patients complained of giddiness and 2 complained of nausea while in Group P, only 4 patient had giddiness**.** These values were not statistically significant .This implies that Pregabalin and gabapentin do not cause any significant side effects**.** In group C, 5 patients had nausea and 3 patients had vomiting. This may be due to increased doses of tramadol in the placebo group.

DISCUSSION

Post operative pain is the reason for several complications like delayed recovery,metabolic alterations,anxiety and stress to the patients and patient dissatisfaction. Hence several studies have been conducted to identify the best methods of providing post operative pain relief. The concept of preemptive analgesia introduced by Crile and further developed by Wall and Woolf revolutionized post operative pain relief[10]. Kehlet and Dahl developed the concept of multimodal analgesia[9] to reduce the dosage of opioids in patients who are at a high risk of developing chronic pain. The main aim of multimodal analgesia is to reduce the dosage and side effects of opioids by replacing with drugs which act by different mechanisms. Gabapentinoids have been found to be very effective in this role . This was the basis of this study .

This study was a prospective ,randomized, single blinded study conducted by the Department of Anaesthesiology, Thanjavur medical college in collaboration with Department of Orthopaedics,.In this study,90 patients undergoing lower limb orthopaedic surgeries under spinal anaesthesia were enrolled and randomly allocated into 3 groups-Group P received Pregabalin 300mg,Group G patients received Gabapentin 900mg and Group C received

placebo. This is similar to a study conducted by Rajendran et al [26], 90 patients undergoing lower abdominal surgeries were selected and allocated into 3 groups (Pregabalin group,Gabapentin group and Placebo group) with similar dosage of drugs.

The study was conducted in orthopaedic patients because orthopaedic surgeries are considered one of the most painful procedures in the post operative period as described by Beaussier et al [27]

DOSAGE OF DRUGS

In this study, oral Gabapentin was given in the dosage of 900 mg and Pregabalin was given in the dosage of 300 mg. This was similar to the study conducted by Rajendran et al. Schmidt et al in 2013[30] evaluated many studies and postulated that higher doses of gabapentin (upto 1200 mg) and Pregabalin (upto 300 mg) were more clinically significant in reducing post operative pain than lower doses. This was the reason why 300mg of Pregabalin and 900 mg of Gabapentin were compared in this study.

Jokela et al[24] observed that analgesia was better after premedication with pregabalin 150 mg in patients undergoing day-case gynaecological laparoscopic surgery. Hence the drugs were given preoperatively in this study.

Paech et al[29] reported that a single preoperative dose of 100 mg pregabalin was ineffective in reducing acute postoperative pain or improving

recovery after minor surgery involving only the uterus. Khan et al[32] studied 175 patients undergoing lumbar laminectomy and found that patients who received either 900 or 1,200mg of gabapentin (either pre- or postoperatively) had lower pain scores throughout the entire first 24h than patients who received either placebo or 600mg of gabapentin.CK Pandey et al[21] conducted a study in 100 patients undergoing lumbar discectomy in which the authors found that patients who received either 600, 900, or 1,200mg of gabapentin had better pain scores at all time points than those receiving either placebo or gabapentin 300mg.This correlates with the findings in this study.

TIMING OF DRUGS:

The drugs were given preoperatively .This is based on the study conducted by Tiippana et al[19] who conducted a meta analysis of 22 trials using gabapentinoids which concluded that a single dose of gabapentin (300 -1200 mg) given 1 to 2 hours preoperatively significantly reduced the post operative pain scores and post operative opioid consumption and opioid related side effects.

The patients in each group received the drugs 1 hour prior to surgery. This is based on the study conducted by Elinor Ben Menachem [12] who reported that the time of maximal plasma concentration of pregabalin was

approximately 1 hour. The time of peak plasma concentration of gabapentin is around 2 to 3 hours(Rose et al) [11].

DURATION OF SURGERY

In all the patients, standard anaesthetic technique was followed. The three groups were comparable in all demographic characteristics (age, sex, height and weight).They were also comparable in relation to ASA physical status and comorbid conditions.

The mean duration of surgery in this study was 129 minutes in group P, 130 minutes in Group G and 128 minutes in Group C. In comparison, the duration of surgery in the study conducted by Rajendran et al[26] in the three groups were 48.17 minutes,46.7 minutes and 45.6 minutes respectively. A similar study was performed by Usha Bafna et al[1] in patients undergoing gynaecological surgeries under spinal anaesthesia in which the duration of surgery was 56.8,57.2 and 57.8 minutes respectively.

VAS Scores

In this study, the patients were educated about the Visual Analogue scoring .VAS scores were measured at 0 hrs,1 hr,2hrs,3hrs,4hrs,6 hrs,9 hrs,12 and 24 hrs after surgery. .

In the immediate postoperative period (0 hr) ,VAS score showed no statistically significant difference between the three groups. This may be due to the effect of spinal anaesthesia.

The mean VAS scores during postoperative period of 1, 2, 4, 6,9, 12 and 24 hours in group P patients were 1.86,1.93,2,2.6,3.36,3,2.83and 3.43 respectively. In Group G patients the mean VAS scores were 1.97, 1.97, 2, 2.76, 2.87, 2.76, 2.56 and 3.26 respectively. In Group C patients the mean VAS scores were 3,4.96,5.1,5.2.5.7,5.4,5.13 and 5.8 respectively. Thus the VAS scores were significantly less in both Groups P and G compared to Group C. This is similar to the results of the study conducted by Rajendran et al[26] which showed significantly less VAS scores in pregabalin and Gabapentin group compared to placebo in the first 24 hrs post surgery.

A study conducted by Agarwal et al[20] evaluated the effectiveness of a single dose of Pregabalin 150 mg pre operatively in patients undergoing laparoscopic cholecystectomy. Patients receiving pregabalin showed significant reduction in VAS scores in the first 24 hrs post surgery which is similar to the results obtained in this study.

In a study conducted by A.Turan et al[14] in patients undergoing abdominal hysterectomy, gabapentin produced significantly lower VAS scores both during rest and movement at 1,4, 8, 12, 16, 20 and 24 hours. A meta analysis of 22 studies conducted by Tiipana et al[19] revealed that in patients

receiving pre operative gabapentin and pregabalin there was a significant reduction in pain scores during the first 24 hours post surgery.

SEDATION SCORES

Postoperatively all patients were assessed for the level of sedation using Ramsay sedation score periodically at 0, 1, 2, 4, 6, 9,12, and 24 hours. The level of sedation was higher in group P and Group G patients compared to Group C upto 6 hours in the postoperative period. According to the study by Rose et al[11], the elimination half of gabapentin in 4.8 to 8.7 hours which correlates with the findings of this study. The mean elimination t1/2 of pregabalin is 6.3 hours and is also independent of dose and repeated drug administration (Ben Menachem)[12] .This was also supported by the findings in this study.

In a study by C K Pandey et al[21] in patients undergoing laproscopic cholecystectomy,it was found that there was higher incidence of sedation (33.98%) in gabapentin group of patients.Ghai et al[17] compared effects of 300 mg Pregabalin and 900 mg Gabapentin in 90 patients undergoing hysterectomy. They reported that the incidence of somnolence was 33% in Gabapentin group compared to control. In the study by Rajendran et al,it was found that both pregabalin had slightly higher sedation scores than gabapentin upto 6 hours post surgery whereas in this study the sedation scores were similar in pregabalin and gabapentin groups.

TIME OF FIRST RESCUE ANALGESIC

Postoperatively all patients were monitored for VAS scores periodically. When the VAS score was 4 or greater, patients were given Tramadol 2mg/kg intravenously as initial dose In this study, it was found that the time interval for first dose of rescue analgesic with tramadol post surgery was 137.8minutes in Control group, 502.3 minutes in Pregabalin group and 382.6minutes in Gabapentin group. The P value was found to be 0.001, which is considered significant. This shows that pregabalin and gabapentin provide prolonged pain relief compared to control. Pregabalin gives significantly longer pain relief compared to gabapentin.This finding correlates with the findings in many other studies.

In a study by Saraswat et al[16], the time from spinal analgesia to first dose of analgesic was 8.98h in Group G whereas 14.17h in Group P, which was highly significant ($P < 0.001$).In the study conducted by Rajendran et al[24], the time for rescue analgesic in control, pregabalin and gabapentin groups were 4.93 hrs,24 and 20.76 hrs respectively. The increased time interval in their study could be because the rescue analgesic was given only when VAS scores were higher than 7 whereas in this study the rescue analgesic was given when VAS score was 4 and above. Moreover, the

duration of surgery in their study was shorter (45.6,46.7,48.17 minutes) compared to this study (129,130.83 and 128.33 minutes).

In the study conducted by Usha Bafna et al[1] in 90 patients undergoing gynaecological surgeries under spinal anaesthesia, the mean duration of effective analgesia in pregabalin group was 535.16 ± 32.86 min versus 151.83 ± 16.21 min in control group and 302.00 ± 24.26 min in gabapentin group .However the duration of surgery in their study were 56 minutes,59 minutes and 57 minutes respectively. Tiipana et al 's meta analysis of 22 studies[19] also gives evidence to the fact that pregabalin and gabapentin provide prolonged significant postoperative pain relief compared to placebo.This concurs with the findings of this study.

DOSAGE OF TRAMADOL ADMINISTERED IN 24 HOURS POST SURGERY

In this study, the mean dosage of rescue analgesic (tramadol) administered in 24 hours was calculated. In group C patients, average dose of tramadol required was 286.7 mg In group P, the dosage required was 170mg.In group G the dosage required was 176.7mg. The P value was found to be 0.0001 which is highly significant.. Hence it was found that total tramadol consumption was significantly lower in group P and group G patients compared to group C.,There is no significant difference between gabapentin

and pregabalin group. .However in Rajendran et al's study, the mean dosage of tramadol was 386.5mg in control, 90.5 mg in pregabalin group and 200.77 in gabapentin group which showed that pregabalin was more effective than gabapentin in reducing opioid consumption post surgery.

In the study conducted by Saraswat et al[16], total dose of analgesics(diclofenac) in first 24h after undergoing surgery under spinal anaesthesia was 62.5mg in Group P(Pregabalin-300mg) and 72.5mg in Group G(Gabapentin 1200mg) and was not significant (P>.05). This is similar to the findings in this study. In a study by C.K.Pandey et al in patients undergoing laparoscopic cholecystectomy the fentanyl consumption was found to be significantly lower in gabapentin group (221μg) than placebo group(355μg) with P value <0.05.There was a 35% less consumption of fentanyl in gabapentin group. Rorarius et al in 2004[31] conducted a study comparing pre operative Gabapentin 1200 mg vs oxazepam in patients undergoing laparoscopic hysterectomy. The post operative fentanyl consumption was 41% less in gabapentin group vs oxazepam.

The findings in this study are different from the results of Ghai et al s study which revealed that pregabalin 300 mg, given orally 1–2 hours before abdominal hysterectomy, resulted in significantly reduced postoperative analgesic requirement compared with gabapentin 900 mg and placebo. Post operative diclofenac and tramadol consumption was 250 +105mg in placebo compared to 152+46mg in pregabalin group and 170+54 mg in gabapentin

group .In a study conducted by Turan et al, gabapentin was found to reduce total tramadol consumption in 24 hours by 36% in patients undergoing abdominal hysterectomy.

INCIDENCE OF SIDE EFFECTS

In this study, side effects were very negligible in both Group P and Group G. This finding is similar to a study conducted by Dirks et al[28]. In a study by C K Pandey et al in patients undergoing discectomy , it was found that incidence of side effects like nausea (5 vs 4) , vomiting (3vs 4) , fatigue (1 vs 0) and dizziness (1vs 0) were found to be similar in Gabapentin group and pregabalin group. Rajendran et al 's study also showed no significant side effects in patients receiving pregabalin or gabapentin.

SUMMARY

- This was a randomized, single blinded study conducted by the Department of Anaesthesiology ,Thanjavur Medical College in collaboration with the Department of Orthopaedics
- 90 patients undergoing lower limb surgeries under spinal anaesthesia were randomized and divided into 3 groups ,Group P, Group G and Group C
- Group P patients received 300mg tablets of Pregabalin orally ,Group G received 900mg tablets of Gabapentin and Group C patients received placebo tablets one hour before surgery. Standard anaesthetic technique was followed in all patients
- Patients were observed at 0 hr,1,2,3,4,6,9,12 and 24 hrs post surgery
- Post operative pain scores (VAS Score) were significantly less in Group P and Group G patients compared to Group C patients at all time intervals.There was no significant difference between the pain scores in Group P and Group G patients
- Group P and Group G patients had higher sedation scores compared to Group C patients upto 6 hours post surgery.There was no significant difference between the sedation scores in Group P and Group G patients

- Time of first rescue analgesic was significantly prolonged in Group P patients (502.3 min) compared to Group G (382.6 min) and Group C (137.8min)
- The total dose of tramadol given in 24 hours as rescue analgesic was significantly less in Group P (170mg) and Group G (176.7mg) patients compared to Group C patients (286.7mg)
- 4 patients in Group P had giddiness as side effect while in Group G 2 patients had nausea and 3 had giddiness. In group C patients 5 patients had nausea and 3 had vomiting.

CONCLUSION

From this study, the following were concluded

- Preemptive Pregabalin and Gabapentin provide good post operative analgesia compared to placebo in patients undergoing lower limb surgeries under spinal anaesthesia.
- Pregabalin(300mg) provides prolonged pain relief compared to Gabapentin(900mg) in the post operative period
- .Pregabalin and Gabapentin reduce post operative opioid requirement in the first 24 hours post surgery.
- Both drugs have minimal adverse effects

BIBLIOGRAPHY

1. Bafna U, Rajarajeshwaran K, Khandelwal M, Verma AP. A comparison of effect of preemptive use of oral gabapentin and pregabalin for acute post-operative pain after surgery under spinal anesthesia. *Journal of Anaesthesiology, Clinical Pharmacology*. 2014;30(3):373-377.

2. Brennan, T. J. Pathophysiology of postoperative pain. *Pain 2011*; 152, S33.

3. Imani F, Rahimzadeh P. Gabapentinoids: Gabapentin and Pregabalin for Postoperative Pain Management. *Anesthesiology and Pain Medicine*. 2012;2(2):52-53.

4. Emerging concepts in post-operative pain management SS Harsoor *Indian J Anaesth*. 2011 Mar-Apr; 55(2): 101–103

5. Steeds,C.E.,**The anatomy and physiology of pain**.*Surgery,* 27 (12) (2009), pp. 507-511

6. Aitkenhead AR, Rowbotham DJ, Smith G, eds (2001) *Textbook of anaesthesia.* Fourth edition. Churchill Livingstone, Edinburgh.

7. Serpell M. (2006) Anatomy, physiology and pharmacology of pain. *Surgery* 24 (10): 350-353

8. The gate control theory of pain. *British Medical Journal*. 1978;2(6137):586-587

9. Kehlet H, Dahl JB. The value of multimodal or “balanced analgesia in postoperative pain treatment. *Anesth Analg* 1993; 77(5):1048-56

10. Vadivelu N, Mitra S, Schermer E, Kodumudi V, Kaye AD, Urman RD. Preventive analgesia for postoperative pain control: a broader concept. *Local and Regional Anesthesia*. 2014;7:17-22.

11. Rose,M.A , Kam,P.C.A (2002) 'Gabapentin:Pharmacology and its use in pain management', *Anaesthesia,* 2002(57), pp. 451-462.

12. Ben ME. Pregabalin pharmacology and its relevance to clinical practice. *Epilepsia* 2004;45:13-8.

13. Fink R. Pain assessment: the cornerstone to optimal pain management. *Proceedings (Baylor University Medical Center).* 2000;13(3):236-239.

14. Turan A, Karamanlioglu B, Memis D, Hamamcioglu MK, Tükenmez B, , *et al.* Analgesic effects of Gabapentin after spinal surgery. *Anaesthesiology* 2004;100:935-8.

15. Hill CM, Balkenohl M, Thomas DW, Walker R, Mathe H,Murray G. Pregabalin in patients with postoperative dental pain.*Eur J Pain* 2001;5:119-24.

16. Saraswat V, Arora V. Preemptive gabapentin vs pregabalin for acute postoperative pain after surgery under spinal anaesthesia. *Indian J Anaesth* 2008;52:829-34.

17. Ghai A, Gupta M, Hooda S, Singla D, Wadhera R. A randomized controlled trial to compare pregabalin with gabapentin for postoperative pain in abdominal hysterectomy. *Saudi J Anaesth* 2011;5:252-7.

18.Montaser A. Mohamed M.D., Ahmed H. Othman M.D., Ahmad M. Abd El-Rahman M.D Analgesic efficacy and safety of peri-operative pregabalin following radical cystectomy:A dose grading study.*Egypt J Anaesth* (2016), http://dx.doi.org/10.1016/ j.egja.2016.10.003

19. Tiippana EM, Hamunen K, Kontinen VK, Kalso E. Do surgical patients benefit from preoperative gabapentin/pregabalin? A systematic review of efficacy and safety.

Anaesth Analg 2007;104:1545-56.

20. Agarwal A, Gautam S, Gupta D, Agarwal S, Singh PK, Singh U. Evaluation of a single preoperative dose of Pregabalin for attenuation of post operative pain after laproscopic cholecystectomy. *Br J Anaesth* 2008;101:700

21. Pandey CK, Priye S, Singh S, Singh U, Singh RB, Singh PK. Preemptive use of gabapentin significantly decreases postoperative pain and rescue analgesic requirements in laparoscopic cholecystectomy. *Can J Anaesth* 2004;51: 358-63.

22. Fassoulaki A, Patris K, Sarantopoulos C, Hogan Q. The analgesic effect of Gabapentin and mexiletine after breast surgery for cancer. *Anesth Analg* 2002;95:985-91

23. Al-Mujadi H, A-Rfai AR, Katzarov MG, Dehrab NA, Batra YK, Al-Qattan AR. Preemptive Gabapentin reduces postoperative pain and opioid demand following thyroid surgery. *Can J Anesth* 2006;53:268-73.

24. Jokela R, Ahonen J, Taligren M, Haanpaa M, Kortilla K. Pretreatment with pregabalin 75 or 150 mg with ibuprofen to control pain after day care gynaecological laproscopic surgery. *Br J Anaesth* 2008;100:834-40.

25. Panah Khahi M. Yaghooti A. A. et el. Effect of pre-emptive gabapentin on post-operative pain following lower extremity orthopedic surgery under spinal Anesthesia. *Singapore Med J* 2011; 51 (12) : 879-882.

26. Rajendran I, Basavareddy A, Meher BR, Srinivasan S. Prospective, randomised, double blinded controlled trial of gabapentin and pregabalin as pre emptive analgesia in patients undergoing lower abdominal and limb surgery under spinal anaesthesia. *Indian J Pain* 2014;28:155-9.

27. New modalities of pain treatment after outpatient orthopaedic surgery M. Beaussier∗, D. Sciard , A. *Orthopaedics & Traumatology: Surgery & Research* 102 (2016) S121–S124

28. Dirks, Jesper et el. A randomized study of effects of single dose Gabapentin versus Placebo on post-operative pain and Morphine consumption after Mastectomy. *Anesthesiology* Sep 2002; 97 (3) : 560 – 564.

29. Paech MJ, Goy R, Chua S, Scott K, Christmas T, Doherty DA. A randomized, placebo-controlled trial of preoperative oral pregabalin for postoperative pain relief after minor gynecological surgery. *Anesth Analg* 2007; 105: 1449–53

30. Schmidt,P.C,* Ruchelli,G , Mackey,S (2013) 'Perioperative Gabapentinoids: Choice of Agent, Dose, Timing, and Effects on Chronic Post surgical Pain', *Anaesthesiology,* (119), pp. 1215-21.

31. Rorarius M.G.F., Mennander S., et el. Gabapentin for the prevention of post-operative pain after vaginal hysterectomy. *Pain* 2004; 110 : 175-81

32. Khan ZH, Rahimi M, Makarem J, Khan RH: Optimal dose of pre-incision/post-incision gabapentin for pain relief following lumbar laminectomy: A randomized study. *Acta Anaesthesiol Scand* 2011; 55:306–12

33. Turan, A ;Memiş, D. (2004). The Analgesic Effects of Gabapentin in Monitored Anesthesia Care for Ear-Nose-Throat Surgery. *Anesthesia and analgesia*. 99. 375-8

34. Verma A, Arya S, Sahu S, Lata I, Pandey H D, Singh H. To Evaluate the Role of Gabapentin as Preemptive Analgesic in Patients Undergoing Total Abdominal Hysterectomy in Epidural Anaesthesia. *Indian J Anaesth* 2008 ;52:428

PROFORMA

NAME: AGE: SEX: IP NO:

HT: WT:

DIAGNOSIS:

SURGERY:

ASA Physical Status:

Co-Morbidity:

SUB ARACHNOID BLOCK

Local anaesthetic given: Dosage of local anaesthetic:

Additives:

Pre- OP:

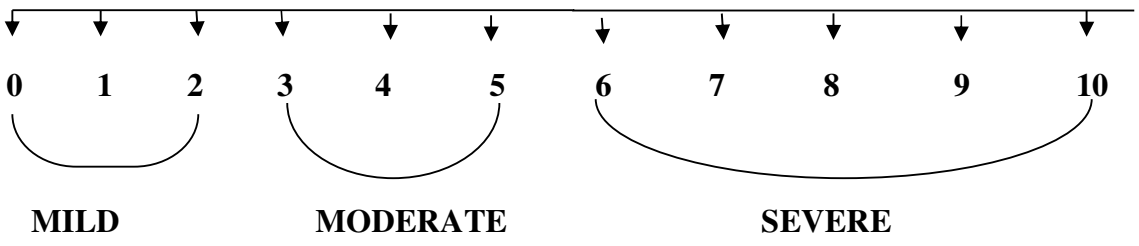
PR: BP: SPO2:

DURATION OF SURGERY :

POST-OP PAIN SCORE (VAS SCORE)

TIME	0 HOURS	3 HOURS	2 HOURS	3 HOURS	4 HOURS	6 HOURS	9 HOURS	12 HOURS	24 HOURS
SCORE									

VAS SCORE



POST OPERATIVE SEDATION SCORE (RAMSAY SEDATION SCORE)

Time	0 Hours	1 hours	2 hours	3 Hours	4 Hours	6 Hours	9 Hours	12 Hours	24 Hours
SCORE									

RAMSAY SEDATION SCALE

AWAKE LEVELS

1 = ANXIOUS, AGITATED;

2 = ORIENTED, CO OPERATIVE, TRANQUIL;

3 = RESPONDS TO COMMAND;

ASLEEP LEVELS

RESPONSE TO A LIGHT GLABELLAR TAP OR LOUD AUDITORY STIMULUS;

4 = BRISK RESPONSE; 5 = SLUGGISH RESPONSE; AND

6 = NO RESPONSE)

TIME FOR FIRST RESCUE ANALGESIC:

RESCUE ANALGESICS IN FIRST 24 HRS

TIME				
ANALGESIC				

COMPLICATIONS:

SNo	Group	Age	Sex	HT	Wt	ASA	Diagnosis	Surgery	Duration	Comorbid	VAS	VAS	VAS	VAS
												0	1	2
1	P	50	M	160	64	1	BB# RT LEG	DFLCP	120	NIL	1	1	1	1
2	P	18	M	158	45	1	# RT FEMUR	ORIF NAIL	135	NIL	1	2	2	2
3	P	45	F	152	60	1	BB # LT LEG	ORIF NAIL	130	NIL	2	2	2	2
4	P	22	M	162	48	1	BB# RT LEG	ILLIZAROV	145	NIL	1	2	2	2
5	P	23	M	160	52	1	INFECTED IMPLANT LT LEG	IMPLANT EXIT	90	NIL	1	1	1	2
6	P	48	F	150	55	2	BB # RLT LEG	ORIF NAIL	145	DM,HT	1	1	2	3
7	P	20	M	165	65	1	BB# RT LEG	ORIF PLATING	140	NIL	1	2	2	2
8	P	46	M	166	60	2	INFECTED IMPLANT LT FEMUR	IMPLANT EXIT	95	NIL	1	2	2	2
9	P	25	M	165	60	2	# LT FEMUR	DHS	155	NIL	1	2	2	2
10	P	24	M	168	70	1	# RT FEMUR	ORIF	150	NIL	1	2	2	2
11	P	47	M	156	50	1	BB# RT LEG ILLIZAROV	CORTICOTOMY RING ADJ	100	NIL	2	2	2	2
12	P	55	M	164	65	2	# RT TIBIA	ORIF NAIL	155	SMOKER	1	2	2	2
13	P	60	M	162	58	2	RT FEMUR # CLOSED	ORIF PLATING	140	SMOKER	1	2	2	2
14	P	55	M	165	54	2	# LT TIBIA	ORIF PLATING	160	SMOKER	2	2	2	2
15	P	57	M	168	65	2	BB # RT LEG	ORIF PLATING	140	SMOKER	2	2	2	2
16	P	50	M	167	64	1	ACL TEAR LT	ARTHROSCOPY	115	NIL	2	2	2	2
17	P	55	M	166	55	2	BB # RT LEG	CORTICOTOMY RING ADJ	100	DM	2	2	2	2
18	P	35	M	158	50	1	PATELLAR #	TBW	120	NIL	2	2	2	2
19	P	36	M	162	60	1	LT FEMUR # LT INTERTROCHANTERIC	DHS	125	NIL	2	2	2	2
20	P	49	M	156	60	1	TRIMALLEOLAR # ANKLE	ORIF PLATING	150	NIL	2	2	2	2
21	P	45	M	155	45	1	BB # RT LEG	ORIF NAIL	110	NIL	2	2	2	2
22	P	46	M	160	66	2	NONUNION # RT TIBIA	ILIZAROV	140	NIL	2	2	2	2
23	P	59	M	161	60	2	# LT TIBIA	ORIF NAIL	115	HT	2	2	2	2
24	P	58	M	164	50	2	BB # LT LEG	ORIF NAIL	130	DM	2	2	2	2
25	P	45	M	164	56	1	BB # RT LEG	ORIF NAIL	105	NIL	2	2	2	2
26	P	34	M	165	60	1	# FEMUR LT	ORIF NAIL	160	NIL	1	1	2	2
27	P	60	M	158	60	2	BB # RT LEG ON ILLIZAROV	REALIGNMENT	95	SMOKER	1	2	2	2
28	P	19	M	163	65	2	BB # RT LEG	ORIF NAIL	135	NIL	2	2	2	2
29	P	59	M	165	62	2	BB # RT LEG	ORIF NAIL	115	SMOKER	2	2	2	2
30	P	24	M	166	64	1	OSTEOMYELITIS RT TIBIA	ILLIZAROV FIXATION	155	NIL	1	2	2	2

SNo	Group	Age	Sex	HT	Wt	ASA	Diagnosis	Surgery	Duration	Comorbid	VAS	VAS	VAS	VAS
31	G	34	M	165	62	1	# RT TIBIA	ILLIZAROV	150	NIL	1	1	1	2
32	G	55	M	158	64	2	BB # RT LEG	ORIF NAIL	130	NIL	2	2	2	2
33	G	19	M	154	52	1	# LT FEMUR	ORIF NAIL	160	NIL	1	2	2	2
34	G	52	M	161	56	2	# LT FEMUR	ORIF NAIL	125	HT	2	2	2	2
35	G	30	M	162	63	1	# LT FEMUR	ORIF PLATING	155	NIL	2	2	2	2
36	G	48	M	165	68	2	BB # RT LEG	ORIF NAIL	135	NIL	2	2	2	2
37	G	22	M	155	62	1	# RT TIBIA	ORIF NAIL	100	NIL	2	2	2	2
38	G	30	M	160	51	2	BB # LT LEG	ILLIZAROV REMOVAL AND CAPSULOTOMY	105	SMOKER	2	2	2	2
39	G	24	M	166	58	1	# LT FEMUR	ORIF NAIL	140	NIL	2	2	2	2
40	G	37	M	160	70	2	CLOSED # LT FIBULA	ARTHROSCOPY	150	DM,HT	2	2	2	2
41	G	19	M	155	55	1	BB# LT LEG	ILLIZAROV	165	NIL	2	2	2	2
42	G	46	M	160	54	2	BB# RT LEG ON ILLIZAROV	ILLIZAROV RING ADJUSTMENT	90	SMOKER	2	2	2	2
43	G	55	M	156	60	1	ANKLE DISLOCATION RT	ANKLE ARTHRODESIS	150	NIL	2	2	2	2
44	G	32	M	163	68	2	RT FEMUR NAIL IN SITU	IMPLANT EXIT	105	SMOKER	2	2	2	2
45	G	31	M	157	59	1	RT FEMUR # CLOSED	ORIF NAIL	120	NIL	2	2	2	2
46	G	57	M	166	70	2	CLOSED # RT INTERTROCHANTERIC FEMUR	NAILING	130	SMOKER	2	2	2	2
47	G	34	M	158	52	1	# RT TIBIA LAT CONDYLE	ORIF PLATING	180	NIL	2	2	2	2
48	G	25	M	158	50	1	# LT FEMUR	ORIF NAIL	135	NIL	2	2	2	2
49	G	18	M	156	49	1	BB # LT LEG	ORIF NAIL	110	NIL	2	2	2	2
50	G	58	M	165	58	2	# RT FEMUR	LRS FIXATION	125	SMOKER	2	2	2	2
51	G	55	M	160	64	2	INFECTED IMPLANT RT LEG	IMPLANT EXIT	100	SMOKER	2	2	2	2
52	G	50	M	156	48	2	CLOSED # RT FEMUR	LRS FIXATION	150	SMOKER	2	2	2	2
53	G	45	M	166	65	2	CLOSED # RT FEMUR	ORIF NAIL	145	SMOKER	2	2	2	2
54	G	51	M	168	68	2	MALUNITED # RT TIBIA	IMPLANT REMOVAL AND LRS FIXATION	160	DM,HT	2	2	2	2
55	G	30	F	156	50	1	# RT FEMUR SHAFT	ORIF NAIL	120	NIL	2	2	2	2
56	G	52	M	167	60	2	# BB RT LEG	ORIF NAIL	135	SMOKER	2	2	2	2
57	G	44	M	163	60	1	# LT TIBIA PLATEAU	ORIF NAIL	125	NIL	2	2	2	2
58	G	18	M	160	48	1	# LT FEMUR SHAFT	ORIF PLATING	120	NIL	2	2	2	2
59	G	27	M	165	63	1	# RT FEMUR SHAFT	ORIF NAIL	155	NIL	2	2	2	2

SNo	Group	Age	Sex	HT	Wt	ASA	Diagnosis	Surgery	Duration	Comorbid	VAS	VAS	VAS	VAS
60	G	51	M	162	60	2	# RT FEMUR INTERTROCHANTERIC	PFN	145	DM,HT	2	2	2	2
61	C	45	M	158	58	1	INFECTED IMPLANT LT LEG	IMPLANT EXIT	100	NIL	2	3	2	4
62	C	33	M	160	60	2	SUBTALAR ARTHRITIS RT ANKLE	ARTHRODESIS	120	SMOKER	2	2	2	4
63	C	60	M	162	65	2	# RT TIBIA	ORIF NAIL	135	SMOKER	2	2	2	4
64	C	56	F	150	48	2	# RT FEMUR SUBTROCHANTERIC	ORIF PLATING	140	DM,HT	2	3	4	2
65	C	28	M	163	60	1	BB # RT LEG	ORIF NAIL	110	NIL	2	2	2	4
66	C	55	M	165	65	2	BB # LT LEG	ORIF NAIL	125	HT	2	2	4	2
67	C	29	M	164	52	1	CLOSED # LT FEMUR IT	DHS	145	NIL	3	4	2	2
68	C	52	M	169	64	2	BB# RT LEG	EXTERNAL FIXATOR	125	HT	2	3	4	2
69	C	36	M	170	70	1	BB # RT LEG	ORIF NAIL	105	NIL	2	2	3	4
70	C	46	M	168	66	2	ACL TEAR RT	ARTHROSCOPY	125	HT	2	2	4	3
71	C	24	M	172	64	1	SHAFT OF FEMUR# RT	ORIF NAIL	135	NIL	2	4	3	2
72	C	60	M	160	60	2	# RT FEMUR INTERTROCHANTERIC	PFN	150	SMOKER	2	4	2	2
73	C	58	M	165	65	2	CLOSED # NECKOF FEMUR	HEMIARTHROPLASTY	135	SMOKER	2	2	4	2
74	C	23	M	158	55	1	# LT TIBIA PLATEAU	ORIF NAIL	120	NIL	2	2	2	4
75	C	56	M	163	58	2	INTERTROCHANTERIC # FEMUR RT	PFN	150	HT	2	4	2	2
76	C	40	M	158	56	2	# RT FEMUR SHAFT	ORIF NAIL	115	HT	2	3	4	2
77	C	40	M	162	57	1	# RT TIBIAL PLATEAU	ORIF PLATING	105	NIL	2	2	3	4
78	C	37	M	165	60	2	# RT FEMUR SUBTROCHANTERIC	DHS	140	DM,HT	2	4	2	2
79	C	25	M	166	64	1	# SHAFT OF FEMUR RT	ORIF NAIL	130	NIL	2	3	4	2
80	C	30	M	165	70	1	# RT FEMUR SHAFT	ORIF NAIL	120	NIL	2	3	5	3
81	C	27	M	163	72	1	BB # RT LEG	ORIF NAIL	90	NIL	2	3	3	5
82	C	50	M	159	62	2	BB # RT LEG	ORIF NAIL	115	SMOKER	2	3	3	4
83	C	27	M	168	64	1	# BB RT LEG	ORIF NAIL	140	NIL	2	3	5	2
84	C	60	F	155	50	2	# LT TIBIA PLATEAU	ORIF PLATING	120	DM	2	3	3	4
85	C	27	M	167	60	2	# BB RT LEG	ORIF NAIL	105	SMOKER	2	2	3	5
86	C	60	M	165	55	2	# BB LT LEG	ORIF NAIL	140	SMOKER	3	4	2	3
87	C	17	M	160	54	1	TIBIAL EPIPHYSEAL INJURY	ORIF PLATING	125	NIL	2	3	3	5
88	C	17	M	162	50	1	# RT FEMUR SPRACONDYLAR	ORIF PLATING	130	NIL	2	3	3	4
89	C	60	M	165	60	2	BB # RT LEG	ORIF PLATING	170	SMOKER	3	5	3	2
90	C	27	M	172	72	1	BB # RT LEG	ORIF NAIL	155	NIL	3	5	3	3

SNo	VAS score	VAS	VAS	VAS	VAS	RAM SAY	RAM SAY	RAM SAY	RAM SAY	RAM SAY	RAM SAY	RAM SAY	RAM SAY	RAM SAY	T1	TRAMADOL 24hrs	NAUSEA	VOMITING	GIDDINESS
	3	4	6	9	12	24	0	1	2	3	4	6	9	12	24				
1	2	2	5	5	6	2	2	2	2	2	2	1	2	1	480	200	A	A	A
2	2	4	3	4	3	2	2	2	2	2	1	2	1	2	360	200	A	A	A
3	2	5	3	4	4	2	2	2	2	2	1	2	1	2	300	200	A	A	A
4	3	4	2	2	4	2	2	2	2	2	1	2	2	1	360	200	A	A	A
5	3	4	3	3	4	2	2	2	2	2	1	2	2	2	360	100	A	A	A
6	3	4	4	3	4	2	2	2	2	2	1	1	2	1	330	200	A	A	P
7	4	2	3	4	2	2	2	2	2	1	2	2	1	2	240	200	A	A	A
8	3	4	3	3	5	2	2	2	2	2	1	2	2	1	350	200	A	A	A
9	4	3	4	3	4	2	2	2	2	2	1	2	2	1	260	200	A	A	A
10	2	4	3	4	3	2	2	2	2	2	1	2	1	2	370	200	P	A	A
11	3	3	4	3	4	2	2	2	2	2	2	1	2	1	540	100	A	A	A
12	3	4	2	3	4	2	2	2	2	2	1	2	2	1	380	200	A	A	A
13	2	3	4	2	2	2	2	2	2	2	2	1	2	2	550	100	A	A	A
14	4	2	2	4	2	2	2	2	1	2	2	2	1	2	250	200	A	A	A
15	3	5	2	2	4	2	2	2	2	2	1	2	2	1	360	200	A	A	A
16	3	4	2	2	2	2	2	2	2	2	1	2	2	2	340	100	A	A	A
17	2	2	4	2	4	2	2	2	2	2	2	1	2	1	530	200	A	A	A
18	2	5	2	2	4	2	2	2	2	2	1	2	2	1	370	200	A	A	A
19	4	2	2	3	4	2	2	2	2	1	2	2	2	1	220	200	A	A	A
20	2	2	4	2	2	2	2	2	2	2	2	1	2	2	530	100	A	A	A
21	2	4	2	2	4	2	2	2	2	2	1	2	2	1	350	200	A	A	A
22	4	2	2	2	4	2	2	2	2	1	2	2	2	2	240	100	A	A	A
23	2	5	2	4	2	2	2	2	2	2	1	2	1	2	350	200	A	A	A
24	2	4	3	3	4	2	2	2	2	2	1	2	2	1	360	200	A	A	A
25	2	2	4	2	2	2	2	2	2	2	2	1	2	2	550	100	A	A	A
26	2	4	2	2	4	2	2	2	2	2	1	2	2	1	370	200	A	A	A
27	2	2	4	2	2	2	2	2	2	2	2	1	2	2	540	100	A	A	A
28	2	4	2	2	4	2	2	2	2	2	1	2	2	1	360	200	A	A	A
29	2	2	4	2	4	2	2	2	2	2	2	1	2	2	520	100	A	A	A
30	2	4	2	4	2	2	2	2	2	2	1	2	1	2	350	200	A	A	A

SNo	VAS score	VAS	VAS	VAS	VAS	RAM SAY	RAM SAY	RAM SAY	RAM SAY	RAM SAY	RAM SAY	RAM SAY	RAM SAY	RAM SAY	T1	TRAMADOL 24hrs	NAUSEA	VOMITING	GIDDINESS
31	3	3	4	3	4	3	3	3	2	2	2	2	2	2	510	100	A	A	A
32	2	4	2	2	4	3	3	2	2	2	1	2	2	1	370	200	A	A	P
33	2	4	2	2	4	3	2	2	1	2	2	1	2	2	360	200	P	A	P
34	2	2	4	2	2	3	3	2	2	2	2	1	2	2	540	100	A	A	P
35	4	2	2	2	4	3	2	2	2	2	1	2	2	2	350	100	A	A	A
36	2	3	5	2	4	3	2	2	2	2	2	1	2	1	500	200	A	A	A
37	2	4	2	2	4	3	3	2	2	2	1	2	2	1	360	200	A	A	P
38	2	2	4	2	2	3	3	2	2	2	2	1	2	2	550	100	A	A	A
39	2	4	2	4	2	3	2	2	2	2	1	2	1	2	350	200	A	A	P
40	4	2	2	2	4	3	2	2	2	1	2	2	2	1	250	200	A	A	P
41	5	3	2	4	2	3	2	2	2	1	2	2	1	2	240	200	A	A	A
42	2	2	4	2	2	3	3	3	2	2	2	1	2	2	530	100	P	A	P
43	2	4	2	4	2	3	2	2	2	2	1	2	1	2	350	200	A	A	A
44	2	2	4	2	4	3	3	2	2	2	2	1	2	1	540	200	A	A	A
45	2	4	2	2	4	3	2	2	2	2	1	2	2	1	380	200	A	A	A
46	2	4	2	2	2	3	2	2	2	2	1	2	2	1	300	200	A	A	A
47	4	2	2	4	4	2	2	2	2	1	2	2	1	1	240	200	P	A	A
48	2	4	2	2	2	3	3	2	2	2	1	2	2	2	350	100	A	A	A
49	2	2	4	2	4	3	3	2	2	2	2	1	2	1	560	200	A	A	A
50	2	4	2	2	4	3	3	2	2	2	1	2	2	1	320	200	A	A	A
51	2	2	4	2	2	3	3	3	2	2	2	1	2	2	570	100	A	A	P
52	4	3	2	4	2	2	2	2	2	1	2	2	1	2	250	200	A	A	A
53	4	2	2	4	4	3	2	2	2	1	2	2	1	1	240	200	A	A	A
54	5	2	2	2	4	2	2	2	2	1	2	2	2	1	230	200	A	A	P
55	3	4	2	2	4	3	2	2	2	2	1	2	2	1	360	200	P	A	P
56	2	2	4	2	4	3	3	2	2	2	2	1	2	1	500	200	A	A	A
57	2	4	2	2	4	3	2	2	2	2	1	2	2	1	400	200	A	A	A
58	2	2	4	2	2	2	2	2	2	2	2	1	2	2	520	100	A	A	A
59	4	2	2	4	4	2	2	2	2	1	2	2	4	4	240	200	A	A	P

SNo	VAS score	VAS	VAS	VAS	VAS	RAM SAY	RAM SAY	RAM SAY	RAM SAY	RAM SAY	RAM SAY	RAM SAY	RAM SAY	RAM SAY	T1	TRAMADOL 24hrs	NAUSEA	VOMITING	GIDDINESS
60	5	2	2	4	4	2	2	2	2	1	2	2	1	1	220	300	A	A	A
61	2	2	4	2	5	2	2	1	2	2	2	1	2	1	180	300	P	A	A
62	2	2	5	3	5	2	2	2	1	2	2	1	2	1	160	300	A	A	A
63	2	2	4	2	5	2	2	2	1	2	2	1	2	1	170	300	P	A	A
64	2	2	4	2	5	2	1	2	2	2	2	1	2	1	110	300	A	A	A
65	2	2	4	2	5	2	2	2	1	2	2	1	2	1	190	300	A	A	A
66	2	2	4	2	5	2	2	1	2	2	2	1	2	1	120	300	A	A	A
67	3	3	4	3	5	2	1	2	2	2	2	1	2	1	60	300	P	A	A
68	2	3	2	4	5	2	2	1	2	2	2	2	1	1	130	300	A	A	A
69	2	2	2	4	5	2	2	2	1	2	2	2	1	1	160	300	A	A	A
70	3	3	4	2	5	2	2	1	2	2	2	1	2	1	125	300	P	A	A
71	2	2	4	2	3	2	1	2	2	2	2	1	2	2	100	200	A	P	A
72	2	4	2	2	5	2	1	2	2	2	1	2	2	1	90	300	A	A	A
73	2	2	2	4	5	2	2	1	2	2	2	2	1	1	140	300	A	A	A
74	2	2	2	2	5	2	2	2	1	2	2	2	2	1	180	200	A	P	A
75	2	2	4	3	5	2	1	2	2	2	2	1	2	1	75	300	A	A	A
76	2	2	2	4	6	2	2	1	2	2	2	2	1	1	140	300	A	A	A
77	2	2	2	4	3	2	2	2	1	2	2	2	1	2	190	200	A	A	A
78	2	2	4	2	5	2	1	2	2	2	2	1	2	1	70	300	P	A	A
79	2	2	2	4	5	2	2	1	2	2	2	2	1	1	135	300	A	A	A
80	2	2	5	3	5	2	2	1	2	2	2	1	2	1	120	300	A	P	A
81	2	2	2	4	5	2	2	2	1	2	2	2	1	1	200	300	A	A	A
82	2	2	2	5	4	2	2	2	1	2	2	2	1	1	190	300	A	A	A
83	2	3	4	3	5	2	2	1	2	2	2	1	2	1	130	300	A	A	A
84	2	2	3	5	5	2	2	2	1	2	2	2	1	1	180	300	A	A	A
85	3	2	2	4	4	2	2	2	1	2	2	2	1	1	180	300	A	A	A
86	2	3	5	3	4	2	1	2	2	2	2	1	2	1	80	300	A	A	A
87	3	3	5	3	5	2	2	2	1	2	2	1	2	1	205	200	A	A	A
88	2	3	3	5	5	2	2	2	1	2	2	2	1	1	170	300	A	A	A
89	2	3	5	3	6	2	1	2	2	2	2	1	2	1	80	300	A	A	A
90	3	3	5	3	4	2	1	2	2	2	2	1	2	1	75	300	A	A	A